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ACADEMIC JOURNAL

March Issue

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"Not Waving But Drowning" by Stevie Smith By Brandon Yoon

"Not Waving But Drowning" by Stevie Smith articulates the life and death of a man submerged under ignorance of the general public. His desperate call for help as he 'drowns' lays parallel with the bystanders misinterpretation of him waving in terms of relief. The irony deepens the tragic depiction of the man's death.

The first line immediately strikes the reader with a sense of apprehension through the 'dead man', notifying them of the grim fate of the protagonist. 'Nobody heard him' introduces the theme of ignorance and hints at the solitude the 'dead man' is facing. Though the 'dead' man is seen lying, moaning. A depiction of how he has perished in the views of society but personally still holding on by a thread with just enough energy to express his distress. 'still' conveys that the man can be saved, but The poem switches to first person in lines 3 and 4 out to the audience, as the pained man clarifies that he was indeed in life threatening pain, and was reaching out for help. The first stanza effectively paints the image of a suffering individual, alone and isolated from the world. It invokes a sense of empathy towards the man throughout the audience as they advance through the poem.

The second stanza introduces the people saying 'poor chap, he always loved larking' this lighthearted diction to describe the man contrasts with the next line 'and now, he's dead' This sudden change in tone onsets a mood of unease as the audience is once more reminded of the dead man. 'It must have been too cold for him, his heart gave way' The public directs attention to the seemingly abnormal, hostile environment as the assailant of the man, quick in drawing conclusions of the incident. They also pinpoint that the weather was exclusively unfavorable towards the man, suggested by the 'for him'. This almost belittles the tragic event of death, further bringing pity.

It may also be a note of how the public was oblivious of the current state of the man, not being able to make out any connections to why the man might have been affected by something other than simple natural force. The stanza portrays the inattentive crowd, unable to comprehend the internal struggles of the dying man.

In the final stanza, the man retorts to the people in his perpetual state of pain, claiming the cold that took him was no irregular occurrence with great assurance, implied by the repeats of the 'nos'. The people's visions, the distress he was under He proceeds to lament himself of being 'much too far out all his life', disconnected from the world and people in it to the point where no one considers him 'alive' and remembered by others. After these lines, (still the dead one lay moaning) could also be interpreted as a lament and regret made by the dying man and not just a call for help, as he himself pities the fact that he himself brought him into this situation.

"Not Waving But Drowning" tackles the question of 'If you as an individual are not known to anyone of your existence, do you really even exist?' Is one considered 'alive' when no one knows of your life and story? Smith discusses the themes of disconnection and depression through the 'man', portraying people in our world who are forgotten, unknown, and otherwise disconnected involuntarily. Through the discussion, the audience relates to the vulnerable man.

The light diction and rhyme scheme of A-C contrasts much with the melancholic themes of depression and disconnection. Ultimately, the extended metaphor of drowning amplifies the mental state caused by depression and other mental illnesses, being a sensory representation of the crushing feeling of utter convalescence as you scrape the surface for help.

From Mao to Modernity: China's Rise in the 21st Century By Ziyi Wei

I. Introduction

In the twenty-first century, the central question framing US foreign policy has shifted from McCarthy's infamous "Who lost China?" to "What is China?" This question encompasses crucial facets of the shifting global order: What are China's motives? What will the consequences be? How should the West respond? *Should* the West respond? Addressing these questions is a prerequisite to resolving the multitude of global challenges today, from climate change and food insecurity to terrorism and nuclear proliferation. This essay first examines China's methods to become the leading superpower. Next, it analyzes the economic, social, and geopolitical implications of Chinese hegemony. Finally, it concludes that a globally dominant China, despite presenting the threat of digital authoritarianism, could foster both economic growth and geopolitical stability.

II. How would China become the leading superpower?

Professor Ian Bremmer at Columbia's School of International Affairs defines a superpower as a nation with sufficient economic, political, and military power to influence global politics (Bremmer, 2015). By these standards, China is not yet the leading superpower. Its gross domestic product lags $4 trillion behind that of the US, its military is geographically limited to Asia and the Indo-Pacific, and political stability within the Chinese Communist Party (CCP) is faltering in the wake of the pandemic (Allison, 2023). Thus, in order for China to reach the status of a "leading superpower," it must gain significant economic and military influence in addition to political legitimacy both domestically and abroad.

The rise of China will be different than that of the US. China already faces a number of rivals, including India, Japan, Taiwan, and the US, who challenge its aspirations of regional primacy. Furthermore, solely relying on regional primacy concentrates the competition for global primacy on what the US usually outperforms on—high-end military competitions—and risks pushing China's neighbors "further into Washington's arms". Thus, rather than forcefully pushing the US military out of the Indo-Pacific and Asian regions, China could establish global leadership by shaping economic, technological, and political institutions (Sullivan and Brands, 2020). Such an approach can be classified as expansion of Chinese soft power, defined as a form of co-option through global appeal (Nye, 1990).

III. Economic implications

The Belt and Road Initiative (BRI) is a core example of Chinese expansion of soft power through economic investments. Launched in 2013, it links over 150 countries through a network of ports, roads, railways, and communication infrastructure (Albert, 2018). The BRI has the potential to place China at the center of global trade, boosting its global economic and political influence (Sullivan and Brands, 2020).

When expanded, the BRI could massively benefit participants by making trade more efficient and accessible, boosting global trade by 6.2%, with corridor economies having 10% higher exports. Exporters globally reap the benefits of reduced trade costs and integrated trade networks, resulting in a net increase in Foreign Direct Investment by 7.6%. As a result of improved trade, BRI-related investments have the potential to create over 400,000 jobs and lift 32 million out of poverty (Ruta et al., 2019; Abrar, 2023). Beyond promoting trade, the BRI also serves as a platform for cooperation on global challenges, such as climate change. The BRI International Green Development Coalition brings together 134 organizations and 26 environmental ministries to spearhead sustainable development (UNEP, 2023). In 2022, the coalition held an international roundtable discussion to showcase significant BRI achievements in sustainable development, such as reduced renewable energy costs in Africa. The discussion also facilitated green development planning through partnerships, including one between the Vulnerable Group of Twenty (V20) countries and BRI members, to fund global investment in green energy (WRI, 2022).

Such developments are just the tip of the iceberg in terms of Chinese leadership. Because expansion of the BRI is central to China's status as the leading superpower, the benefits of economic growth and sustainability would be seen across the rest of Eurasia and Africa. By fostering broader technological, financial, and diplomatic cooperation, China can utilize its position to fill the vacuum of climate leadership and help achieve global climate goals (Tsafos, 2022).

There would also be many domestic implications of an expanded BRI. First, foreign investment maximizes innovation output of Chinese enterprises by providing capital, increasing overall investment in domestic research and development (Ito et al., 2012). Investment also intensifies market competition through the entry of foreign capital, which incentivizes companies to innovate for competitive advantages (Amiti and Konings, 2007; Goldberg, et al., 2010). This cycle of innovation provides sustained economic growth and a pathway towards societal development. Secondly, China's overseas lendings to fund BRI projects sterilize dollar inflows produced by trade, depreciating the Yuan and sustaining China's export-driven economy "faster and longer than it otherwise would have" (Chang, 2022). Such economic stimulation is the catalyst for domestic growth, providing the necessary resources for job creation, urbanization, social security, and green development (Whyte, 2021).

IV. Technological and social implications

Beyond substantial expansions in the economic sphere, China must also sustain a technological edge as the leading superpower. Fortunately for China, it is poised to displace the US as the global technological superpower given its leadership in 37 out of 44 crucial technologies, including robotics, artificial intelligence (AI), and biotechnology (Gaida et. al 2023). Chinese technological advancements could bring global benefits in a variety of sectors. In agriculture, research led by Huazhong University found that perturbing the OsKRN gene in rice increases yield by up to 10%, a discovery that helps meet global food demands through

genetically modified crops (Zhu, 2023). In medicine, extensive investment in biotechnological research fueled rapid development of drugs, such as I-Mab Biopharma's anti-CD47 monoclonal antibody, which has the potential to cure leukemia (Han, 2021). In transportation, China debuted a magnetic levitation train that runs at a record 600 km/hr, setting the standard for future, pollution-free travel (Marcus, 2021). China will likely expand its technological investments in pursuit of overall hegemony, forwarding revolutionary breakthroughs and improving quality of life for millions.

Unfortunately, Chinese technological advancements are a double-edged sword. Developments in data collection and intelligence tracking provide the CCP improved capabilities to surveil its citizens (Khalil, 2020). For example, the CCP uses AI, digital currency, and other technology to collect personal information on Xinjiang inhabitants (Human Rights Watch, 2019). This data is used to report "suspicious" activities and imprison Uyghur Muslims to reeducation camps, where they are subject to sterilization, forced labor, and human rights abuses (Maizland, 2022). Digital authoritarianism also plagues millions of Chinese citizens through China's social credit system, which ranks people to promote social integrity (Yang, 2022). Punishments for low credit include slow internet connection, exclusion from education and work, and even public blacklisting (Mistreanu, 2018). Because China lacks a central algorithm to determine social credit, information regarding citizens is gathered through mass surveillance and data collection. Such widespread data collection results in the formation of what Law Professor Anne Cheung at the University of Hong Kong calls a "data state": an authoritarian governance model enabling the state to monitor, evaluate, and control its subjects, leaving no room for autonomy (Cheung and Chen, 2021).

As the world's leading superpower, there is no doubt China will export its digital authoritarianism globally. Corporations like Huawei, Baidu, and Alibaba are already developing global infrastructure for AI, communications, and 5G networks (Hussain et al. 2023). The main concern is standard-setting; modern global competition within the ongoing fourth industrial revolution will let countries set technological standards for generations to come, which Beijing will not hesitate to take charge of. Huawei is one example of a corporation that establishes Chinese technological dominance through standard-setting. Huawei is far more advanced in facial recognition, analytic capabilities, and video surveillance than Samsung or Nokia (Feldstein, 2020). In fact, research found that 75 out of 176 countries deployed AI surveillance, and Huawei-led firms were the leading global suppliers of such technology. China provides the equipment for governments in Uganda, Venezuela, and Cuba to surveil their citizens and quell political challenges (Feldstein, 2019). Furthermore, because the CCP can freely exercise its ability to pressure, censor, and surveil its companies, authoritarianism inevitably permeates the ever-expanding realm of technology. Lack of a free press and rule of law significantly hinders the ability to hold political parties accountable for abuses, reinforcing China's win-win diplomacy; recipient countries acquire systems to control their populations, and in return, China entrenches its global influence (Wang, 2021).

V. Geopolitical implications

China is highly unlikely to rely on military force to become the leading superpower. Some tensions will inevitably arise, but are unlikely to escalate to war. In 2020, for example, Sino-Indian tensions spiked after a deadly clash along the Galway Valley border. Despite both countries strengthening their military presences, peace has persisted, because China knows an unstable South Asia would threaten BRI investments and undermine its international image (Dalton et al. 2020). The same is true for Taiwan: despite heightened tensions after US Representative Nancy Pelosi visited the island in 2022, the economic and political threat of Western sanctions ensures the CCP is unlikely to initiate conflict (Stavridis, 2022). Therefore, despite common narratives of the Thucydides Trap—that war becomes likely when one rising power displaces the current ruling power—restraints in the international order prevent escalation (Allison, 2017). Firstly, China and the US are connected through a global network of institutions, such as the United Nations Security Council, the World Trade Organization, the World Health Organization, and the G20, that have an incentive to promote diplomacy and prevent conflict. Additionally, as demonstrated through Taiwan, the integrated nature of the global economy incentivizes China to avoid high-risk behavior that could potentially lead to war (Thorton, 2022; Yan, 2018). Finally, the threat of nuclear retaliation reinforces the notion of mutually assured destruction, disincentivizing escalation (Thorton, 2022).

History proves that, if anything, Chinese geopolitical leadership will promote global cooperation. Many failures of the western-centric international system have revealed themselves: "endless Middle Eastern wars, the rise of ISIS, and a revanchist Russia," to name a few (Ashford et al., 2019). China has the potential to rebalance the international order by exporting the foundational aspects of Chinese socialism—cooperation and mutual learning—globally. China initiated inclusive international diplomacy through the Association of Southeast Asian Nations, G20, BRIC, and other forums to facilitate common development (Shen, 2018). As the leading superpower, China can break the Western monopoly on global development by transforming international institutions like it has done. Promoting usage of these forums legitimizes them on the international stage, allowing other countries to hold China accountable for humanitarian abuses and setting the precedent for ethical governance that addresses 21st century challenges.

VI. Conclusion

What is China? The answer varies. The Encyclopedia Britannica posits China as "one of the great cradles of world civilization," and yet US intelligence leaders believe China is "the most consequential threat" to national security (Young, et al., 2023; Gazis and Yilek, 2023). To understand China's role in global relations, this essay focused on the domestic and international implications of China as the leading superpower. First, it established a framework for how China must deploy a mixture of co-option and coercion to attain such status. Next, it analyzed the social, economic, and geopolitical implications of Chinese hegemony. Economically, through expanded investments, Chinese leadership yields immense potential for growth. Socially, despite how expanded Chinese influence in the technological sphere advances societal development,

lack of ethical regulations threatens to increase human rights abuses through global digital authoritarianism. Geopolitically, Chinese leadership has the potential to replace centuries of an exclusive, western-centric international system with a model of inclusive global governance and international forums.

Countries cannot be perfect. The US may spearhead global medical research, but it also has 57 times as many school shootings as G7 nations combined (Grabow and Rose, 2018). China possesses the potential to shape the future of global governance for good, yet carries out egregious human rights violations. Regardless of the implications of Chinese hegemony, the crucial question that shapes future policy-making should instead be what global leaders can do to ensure ethical and sustainable governance.

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Characterization of How Microplastics and Processed Foods Affect the Human Microbiome By Dean Jasser

Abstract

Since the advent of the Industrial Revolution across the world, there has been an unprecedented increase in the production of manufactured goods, many of which have been revealed to be harmful to the environment, including the accumulation of microplastics and increased consumption of processed foods. Recently shown to contribute to human disease, the rate of plastic production has quadrupled over the past thirty years [1]. Consumption of processed foods has also increased significantly, with ultra-processed foods making up around 57 percent of an American individual's diet in 2018 [2], leading to adverse effects on human health. Despite the investigation into the effects on the environment and nutritional health these products have, how these products affect the human microbiome is not well understood. Here, we aim to compile previously published human microbiome data from various parts of the world to review and compare the composition and levels of microbes with the specific environmental contaminants listed previously, as well as propose possible solutions and efforts to reduce the negative consequences of these products. Finally, we tested *in vitro* how microplastics affect bacterial growth and initially found no evidence of growth defects when microplastics levels were low and some evidence of growth inhibition when microplastics levels were high. Yet, we hypothesize that the environmental changes that we explore here affect human gut microbiome composition and levels of specific microbes, and that microplastic consumed over time and/or in high amounts may negatively affect the health of the human microbiome. To better treat disease induced by bacterial imbalances or infections, it is important to understand how human-induced environmental changes affect the human microbiome and therefore ultimately human health long-term.

Keywords
microbiome, microplastics, processed foods, gut bacteria, bacterial homeostasis

Introduction
Human gut microbiota largely include Firmicutes, Bacteroidetes, and Proteobacteria.

The human gut is home to over one hundred trillion microorganisms that range from bacteria to fungi to parasites to viruses [3]. Bacteria, specifically, provide many of the necessary functions to maintain the human body. These include stimulating the immune system, breaking down toxic food compounds, and synthesizing vitamins and amino acids [4]. Bacterial populations within the body have been shown to be vulnerable to changes in diet, pharmaceutical drugs, geography, stress, infant feeding methods, birthing process, and general lifestyle changes [5]. Despite the multitude of different factors that contribute to an adaptable microbiome, little is known about the effects of microplastics on the gut bacteria. In a similar way, there remains a lot to uncover on the relationship between processed foods and the microbiome.

Among three of the main intestinal bacterial species are Firmicutes, Bacteroidetes, and Proteobacteria. Firmicutes make up well over thirty percent of the microbiome, are Gram-positive, and are typically either rod-shaped or circular bacteria. These bacteria are capable of metabolizing and digesting complex carbohydrates the body cannot. However, Firmicutes are often regarded as 'bad' bacteria, due to their negative influence on the metabolism of glucose and fat [6, 7]. At the same time, Firmicutes have been shown to produce butyrate, which is a short-chain fatty acid that contributes to anti-cancer and anti-inflammatory functions [8]. Together, Firmicutes and Bacteroidetes species make up over ninety percent of the total gut microbiome. Microorganisms that belong to the Bacteroidetes phylum are generally rod-shaped, gram-negative bacteria. Interestingly, they are also commonly associated with reducing inflammation [6]. The relationship between these two types of bacteria determines a lot about a person's health. An excessive increase or decrease in the ratio between the two has been observed with cases of diabetes and inflammatory bowel disease, respectively [7]. Last, Proteobacteria are gram-negative, and are not usually categorized by a single shape. Many Proteobacteria use a flagella for motility [9]. Proteobacteria have been found to be a microbial signature of disease, such as asthma, chronic obstructive pulmonary disease, inflammatory bowel disease [10]. These published data therefore suggest that Proteobacteria may have proinflammatory properties. Therefore, it is important to understand how the balance of these species is maintained and how human health may be affected under conditions known to disrupt the microbiome.

High levels of microplastics are consumed by humans in many different parts of the world.

Microplastics are defined as plastic pieces that are less than five millimeters in length. Additionally, plastics that are less than one nanometer long are classified as nanoplastics. Studies have shown that roughly one hundred and sixty thousand tons of primary microplastics are manufactured in Europe each year, and over fourteen million tons of microplastics have accumulated upon the world's ocean floor. [11]. These microplastics range from microbeads and plastic pellets to tire abrasions from automobiles and microfibers released during the washing of synthetic textiles. These microplastics can be found in marine water, freshwater bodies, agroecosystems, the atmosphere, food, drinking water, and many other places. In fact, microplastics have found ways to invade even the places thought to be most sterile and protected, such as the lungs, blood, feces, and placenta of unborn children [12]. Many ingested microplastics arrive in the body through the lungs as inhaled nanoplastics. These lung plastics can cause lung irritation, cancer, headaches, and asthma [12]. Plasticizers, a material found in many common plastics to increase their flexibility, have also been proven to disrupt normal hormonal functions, causing higher risks of obesity, cardiovascular disease, reproductive disorders, and breast cancer [13].

In cases of trials where microplastics were fed to Japanese quail chicks, these chicks displayed delayed growth. Researchers believe this to be caused by the endocrine-disrupting chemicals found in microplastics [12]. Additionally, in laboratory tests, microplastics have also

been found to cause damage to human cells, by means of allergic reactions and cell death [12]. In the case of bacteria, studies have shown that microplastics affect both the composition and function of sediment microbial communities, such as the rate of both nitrification and denitrification [14]. Taking all of this into account, the goal of this study is to understand how mild amounts of inhaled microplastics might affect the homeostasis of the human microbiome. We predict that these microplastic dependent disruptions may contribute to adverse human health outcomes (Fig. 1).

High consumption of processed foods leads to gut microbiome abnormalities.

Processed foods, by definition, are any raw agricultural commodities that have been washed, milled, cut, cooked, heated, cooked, frozen, dried, mixed, packaged, dehydrated, canned, pasteurized, chopped, or cleaned [15]. Many foods that fall into this "processed" category are simply minimally processed foods that are prepped for convenience. On the other hand, ready-to-eat foods such as frozen, premade, boxed, or packaged foods are categorized as heavily processed. Foods with artificial sweeteners, spices, oils, preservatives, and colors also fall under the category of highly-processed foods [15]. Over the past decades, developed countries have begun to make the drastic shift to increasing production and consumption of processed foods. In 2013, U.S. processed food exports surpassed forty five billion dollars in revenue, compared to the twenty nine billion dollars made in 2009 [16]. Within the U.S. the average percent of energy intake from ultra processed foods is 57.9% [17]. Due to the availability as well as the affordability of many ultra processed foods, they have become a staple within the diet of many Americans.

As a result of the high consumption of processed foods in American diets, scientists have begun studying what effects these foods may have on the gut microbiome. Using mouse models, in which a cohort of mice was fed exclusively ultra processed foods, researchers found that these mice had abnormal microbiomes when compared to normal mice. Specifically, these mice contained a higher abundance of Bifidobacterium, Parasutterella, and Actinobacteria. Bacteroidetes and Firmicutes expression was also lower in the ultra processed food group. The experimental mice also presented a higher body weight compared to the control group suggesting adverse effects of microbiome changes. This, alongside the negative effects on bone content and overall length of the mice, led to the conclusion that a highly processed diet causes significant aberrant growth in mice [18]. Through this study, we aimed to review known interactions between the microbiome and the amount of processed food in one diet to begin to understand how these foods alter microbiome balance (Fig. 1).

Multiple previous studies demonstrate the importance of microbial homeostasis in human health. For example, a disruption to the normal ratio of Firmicutes to Bacteroidetes has been linked to a multitude of human diseases such as diabetes and inflammatory bowel syndrome [7]. Further, the duodenum contains part of the microbial population that contributes to immune and metabolic diseases. Therefore, delivery of duodenal fecal microbiota has proven to alleviate cases of metabolic syndromes and autoimmune diseases. Interestingly, as a tool, *Lactobacillus*,

either alive or dead, has been shown to affect the human immune response [19]. Bacterial strains such as *Akkermansia muciniphila* correlate negatively with obesity related parameters [20]. Type 2 Diabetes has also been linked to impaired gut microbiome in Asian and European populations. Several studies have implied that the gut microbiome affects glucose regulation, and specific microbial species correlate with insulin resistance [19]. Conclusively, while there are many known diseases caused by microbiome disruptions, there remains much to be discovered and understood about how microbial populations interact to protect against and also induce disease. This has become especially important to study in the context of our changing external environment.

Methodology

Aim of the study: Do microplastics affect the growth of specific gut microbiome bacteria?

Hypothesis: I hypothesize that the environmental changes that we explore here affect human gut microbiome composition and levels of specific microbes, and that microplastic consumed over time and/or in high amounts may negatively affect the health of the human microbiome.

Research design: The research completed was experimental based on what we learned about microbiome and processed food correlations as well as microbiome and microplastics correlations from previously published data [21,22,23]. For the experiment, we wondered how microplastics within an agar plate (an ideal bacterial growth environment) may affect the growth of specific probiotic species. The independent variables were the amount of bacteria inoculated, the amount of microplastics in the plate, and the temperature at which the bacteria grew. The dependent variables were the amount of bacterial growth observed over time.

Scales/ tools/ instruments used:
1. Softwares:
   a. Biorender
   b. Graphpad
   c. Photopea
   d. Iphone camera
2. 4 probiotic pills (~112.5 billion bacteria per pill)
   a. L. plantarum (Gram positive), L. acidophilus, L. paracasei, L. delbrueckii, S. thermophilus, B. longum (Gram. positive), B. breve, B. infantis 8 plates, 8 samples of agar
3. Microscope
4. Incubating chamber (if available)
5. Water
6. 1 mL pipette

7. Pipette controller
8. 10 mL pipette tip
9. LB agar
10. Glassware to make LB
11. Petri dishes
12. Spreaders
13. Cheese grater
14. Pure Leaf Iced Tea plastic bottle
15. Electronic scale

Data Collection Procedure - Experiment 1:
Day 0:
1. Took a plastic bottle, grinded it on a cheese grater for 5-15 minutes.
Day 1:
1. Heat LB agar.
2. Divide the amount you made in half.
3. Add microplastic to plates
4. Pour 10 mL agar into petri dishes → 2 plates total: 1 with 0.1 grams microplastics and 1 with 0.6 grams microplastics.
5. Open 2 probiotic pills using your hands and pour in a 25 mL beaker.
6. Mix thoroughly with a glass stir rod.
7. Dip the spreader within the mixed solution.
8. Use a spreader to spread bacteria around the plate .
9. Place plates on the windowsill.
Subsequent days:
1. Check everyday, take photos of plates after 1 week
2. Take any notes on visual observations (i.e. weird coloring, weird smells, different shaped bacteria on plates)

Data Collection Procedure - Experiment 2:
Day 0:
1. Took a plastic bottle, grinded it on a cheese grater for 5-15 minutes.
Day 1:
2. Heat LB agar.
3. Divide the amount you made in half.
4. Add microplastic to the plate.
5. Pour 20mL agar into petri dishes → 2 plates total: 1 with no microplastics and 1 with 1.8 grams microplastics.
6. Open a singular probiotic pill using your hands and pour in a 25 mL beaker.
7. Mix thoroughly with a glass stir rod.

8. Place 250 microliters of the solution on each plate.
9. Use a spreader to spread bacteria around plates.
10. Place plates on the cabinet.

Subsequent days:

11. Check after 1 and 5 days, observe and take pictures.
12. Take any notes on visual observations (i.e. weird coloring, weird smells, different shaped bacteria on plates)

Fig. 1: The Intestinal Microbiome (middle) can be affected in a multitude of ways, from ways discussed here like processed foods (bottom left) and microplastics (top left), but also from other insults such as medicine use (bottom right) and chemical exposure, such as pesticides (top right).
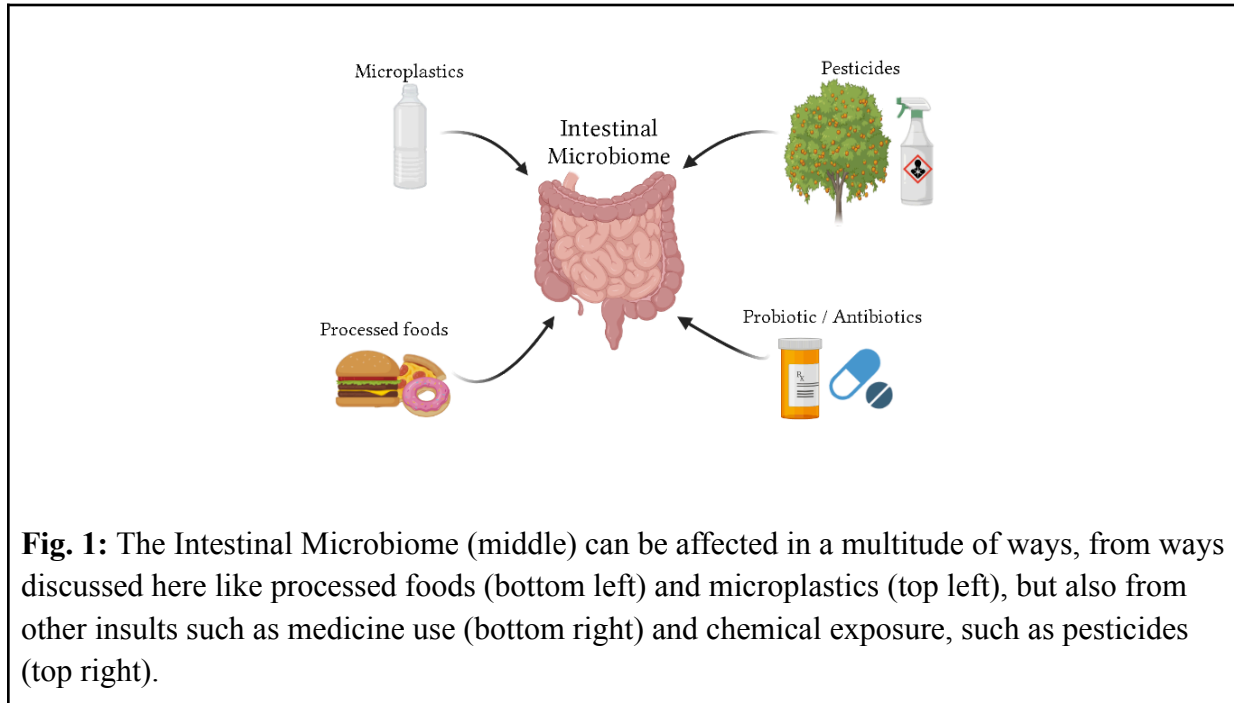
Results

Here, we aim to review current published correlations on microbiome compositions with the amount of processed foods or microplastics in the diet. We investigated this through performing an in-depth literature search on microbiome data from countries with the highest and lowest amounts of processed food or microplastics consumption. We plotted the key findings from these papers (Fig. 2 and Fig. 3) and speculate on how this data may inform public health responses to minimize adverse human health consequences. Prior to completing the research for this paper, we predicted that higher amounts of processed food will increase Proteobacteria, as well as create a negative Firmicutes to Bacteroidetes ratio. In addition, we predicted that exposure to microplastics will increase Firmicutes levels but hinder general gut bacterial growth. A possible explanation for the Firmicutes resilience in both scenarios is their ability to break down more complex carbohydrates, an ability that we thought may also be beneficial in breaking down and thriving in microplastics [4]. Finally, we took our findings to the lab by exposing Lactic acid bacteria including *L. plantarum, L. acidophilus, L. paracasei, L. delbrueckii, S.*

thermophilus, B. longum, B. breve, B. infantis to varying levels of microplastics to evaluate growth defects (Fig. 4). Surprisingly, we did not observe a difference in bacterial growth between the agar plates containing 0.1 g and 0.6 g of microplastics (Fig. 5). Yet, we did observe a small bacterial growth inhibition effect when grown with 1 g microplastics (Fig. 6). We speculate that higher amounts of microplastics are necessary to inhibit growth and predict that the low levels used here may be sufficient to induce changes in bacterial composition of the gut microbiome if administered over time, and may perhaps target species we are unable to test at this time.
We first aimed to review known relationships between processed foods and gut bacteria.

To accomplish this, we researched which countries have reportedly lowest amounts of processed food consumption. We next compared microbiome data from those countries with microbiome data from countries that consume the highest amounts of processed foods. Upon research into comparing published microbiome analysis from both Italy and U.S. stool samples, an interesting pattern emerged. The U.S. stool samples showed a lower level of both Firmicutes and Bacteroidetes, but a higher percentage of Proteobacteria (Fig. 2). The U.S. samples also had a slightly higher Firmicutes to Bacteroidetes ratio [21,22]. While there are confounding factors that may contribute to these differences, we believe the changes reported here warrant further investigations into how processed foods may work in altering the composition of bacteria inside the human gut. Interestingly, a western diet (typically high in fat) is expected to increase both the level of Firmicutes and Proteobacteria. Yet, a Mediterranean diet which Italy generally follows is defined by also having a significant effect on Firmicutes levels within the gut. A Mediterranean diet, which consists of many natural fiber and resistant starch, increases levels of complex carbohydrate digesting Firmicutes. The Mediterranean diet has also been proven to increase levels of bacteroidetes [23]. Taken together, it is likely that processed food consumption differences between Italy and the U.S. play some role in the differences observed in bacterial species in the human gut. The other important detail to note within the comparison is the vastly different levels of proteobacteria within the two countries (Fig. 2). A western diet is linked with an increase in Proteobacteria population. These Proteobacteria carry bacterial lipopolysaccharides within their outer membranes, which serve as endotoxins. These high levels of endotoxins brought on by Proteobacteria and other certain Gram-negative bacteria can lead to both inflammation and insulin resistance [23]. Therefore, it would be interesting to study in the lab whether decreasing the amount of processed foods consumed results in a decrease in endotoxins in the body. Further, this could serve as a method of lowering inflammation in diseased and healthy individuals.
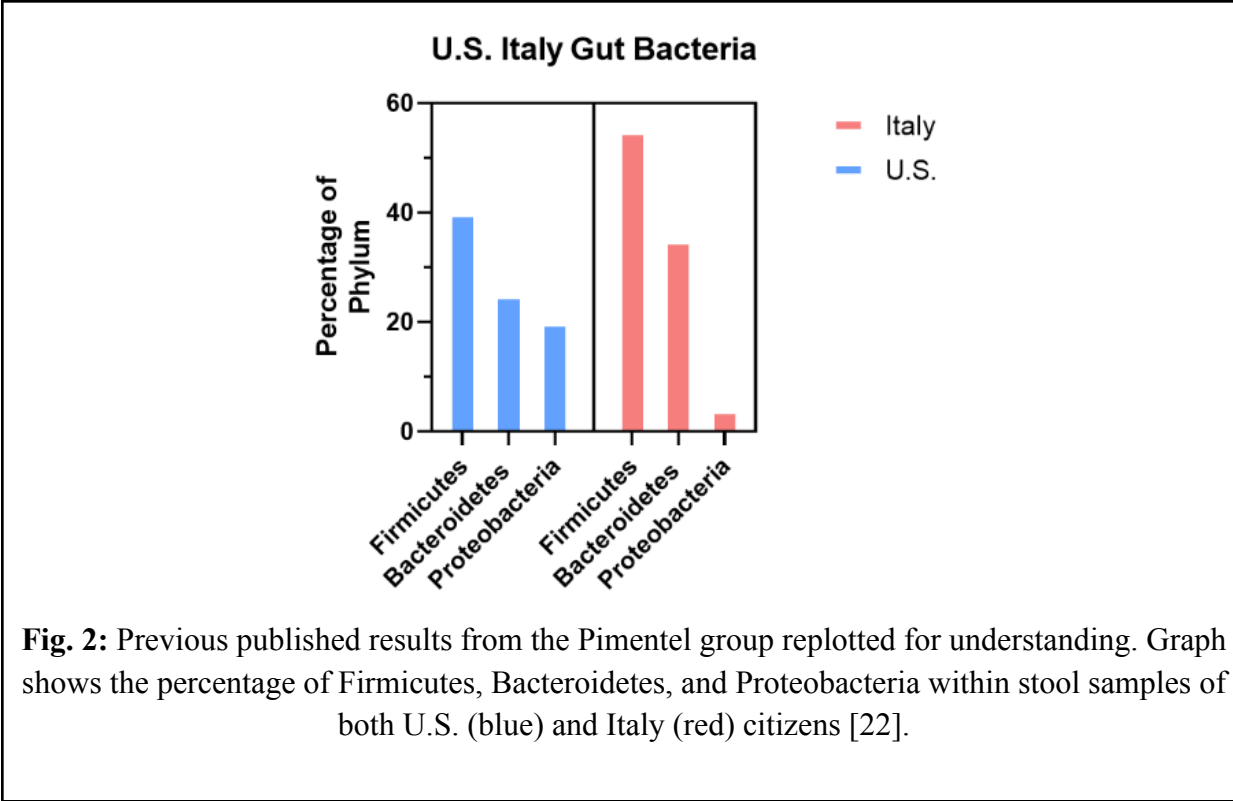
Fig. 2: Previous published results from the Pimentel group replotted for understanding. Graph shows the percentage of Firmicutes, Bacteroidetes, and Proteobacteria within stool samples of both U.S. (blue) and Italy (red) citizens [22].

To increase research rigor, we aimed to compare the published microbiome data from an additional country. Compared to the U.S, India has been shown to favor healthier, less processed foods. While Americans were reported to likely associate the word "tasty" with unhealthy, processed foods, people from India associate taste with spice and favor homemade, less processed foods that are aligned with an ideological idea of naturalness [24]. With this in mind, we observe a high Firmicutes to Bacteroidetes Ratio in the U.S. compared to India (Fig. 3) [21].

Fig. 3: Previous published results from the Balamurugan group replotted for understanding. The median of the Firmicutes to Bacteroidetes ratio within the U.S. and India. As seen, the approximate ratio in the U.S. was 2:1, while India's was roughly 1:2 [21].
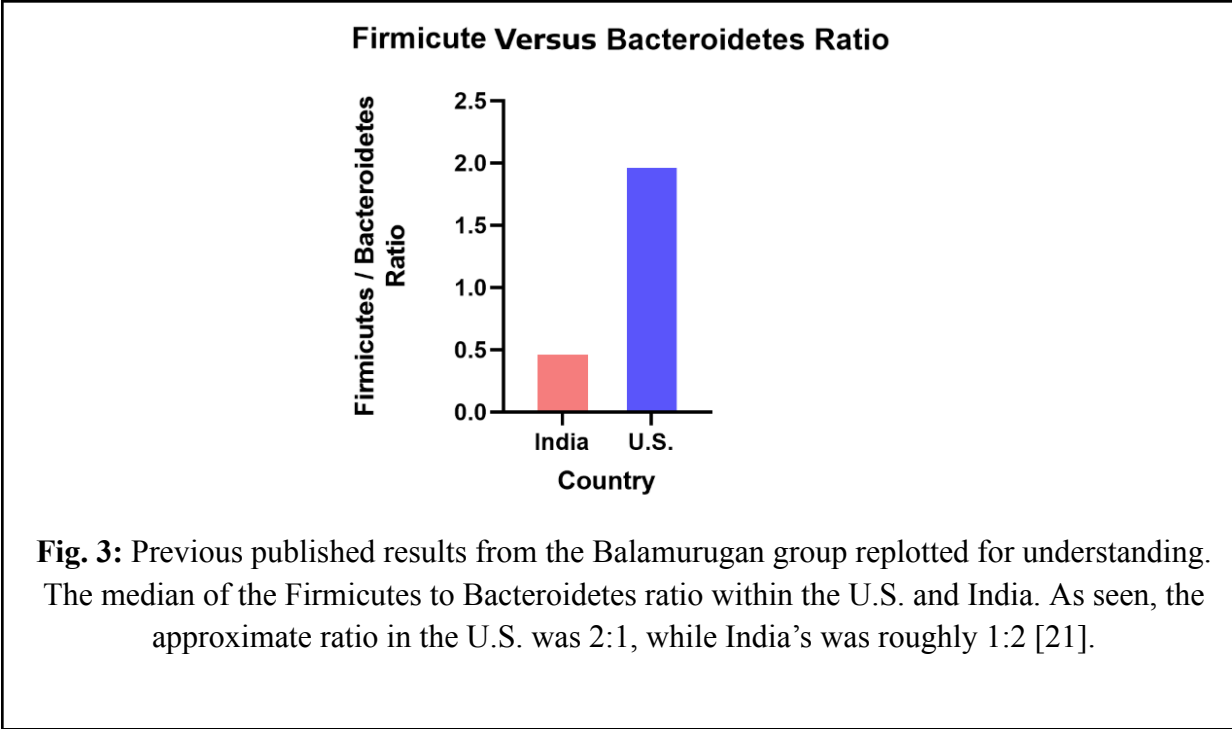
Corresponding to the radically different eating habits of the two countries, the ratio between Firmicutes and Bacteroidetes is likely affected by diet, although we do recognize that other variables such as age, sex, activity level, and genetic predisposition may contribute as well. Intriguingly, a higher Firmicutes to Bacteroidetes ratio has been linked to Diabetes and IBD [7]. Between India and Italy, an interesting comparison arises. Despite the lower amounts of processed foods in both countries, their Firmicutes to Bacteroidetes Ratio are incredibly different. While a high fat diet associated with American food has been proven to increase Firmicutes, the mostly vegetarian diet of India and the Mediterranean diet of Italy each have their own effects on the microbiome [21, 22]. In studies of African children who followed a similar plant-based diet to that of India, lower levels of Firmicutes were found when compared to that of more Western diet-consuming European Children [25]. Yet, in Italy a higher amount of fiber-degrading Firmicutes is observed and therefore accounts for the higher ratio. However, with stricter adherence to the Mediterranean diet, an increase of Bacteroidetes has also been noted by researchers [25].

In a more complicated and less understood way, microplastics affect the human gut microbiome. Interestingly, many of the changes reported thus far investigate bacteria at the genus level. Data has shown that exposure to plastics like silicone-resin, polyurethane, and polyethylene can cause bacterial shifts within the gut [26]. These shifts include the increase of bacteria, such as *Ruminococcus, Dorea, Fusobacterium, and Coprococcus*. These bacterial changes have been linked to increased risks of IBD, colorectal cancer, liver tumors, diarrhea, and gastric inflammation. At the same time, more beneficial bacteria like *Bifidobacteria,*

Streptococcus, and Sphingomonas are sometimes associated with anti-inflammatory, immune-enhancing, and anti-IL-6 benefits [26].

Another important shift we found during our review within the intestinal gut microbiome observing a decrease of Bacteroides and increase of Prevotella within groups with high exposure to microplastics. Bacteroides experienced a drop in abundance by 2.7%, while Prevotella experienced an increase of 5.1%. Bacteroides are known to have antioxidant and beneficial effects on the body [26]. On the other hand, Prevotella are inflammophilic pathobionts who are attracted to and thrive within an inflammatory environment [27]. A higher concentration of Prevotella, therefore, has been assumed to promote inflammatory diseases of the gut.

It has been previously reported that the U.S. and China have varying levels of Prevotella and Bacteroides, which may correlate with the varying levels of plastic and microplastic exposure within the two countries. China, which has been associated with some of the highest levels of plastic in rivers in recent years, had a genus makeup of over 20% Prevotella and approximately 14% Bacteroides. On the other hand, the U.S. has a makeup of around 10% Bacteroides and 5% Prevotella [28,29,30]. This, however, is not definitive evidence between the relation of microplastics and the microbial genus of the gut. There has been a general correlation between Western countries and lower levels of Prevotella when compared to Eastern countries [31]. Still, it is something to keep in mind for further investigations and future study designs.

To better understand how microplastics might inhibit the growth of specific gut promoting bacteria, we designed and executed an *in vitro* experiment (Fig. 4). We first gathered the materials needed for the experiment. We obtained 2 probiotic pills, containing over 112 billion bacteria, which included *L. plantarum, L. acidophilus, L. paracasei, L. delbrueckii, S. thermophilus, B. longum, B. breve, and B. infantis*. We also prepared 2 hard agar plates, both 10 mm in diameter. To do this, 19.3 grams of agar solution was also prepared to fill the rest of the plate, alongside the plastic. The plastic itself was acquired by taking plastic bottles - specifically, Pure Leaf Unsweetened Tea bottles - and grinding them down to small pieces using a cheese grater. These pieces were smaller than 1 millimeter, to properly qualify as microplastics. We also used water and bacterial swab sticks, and a scale to measure the mass of the plastics.
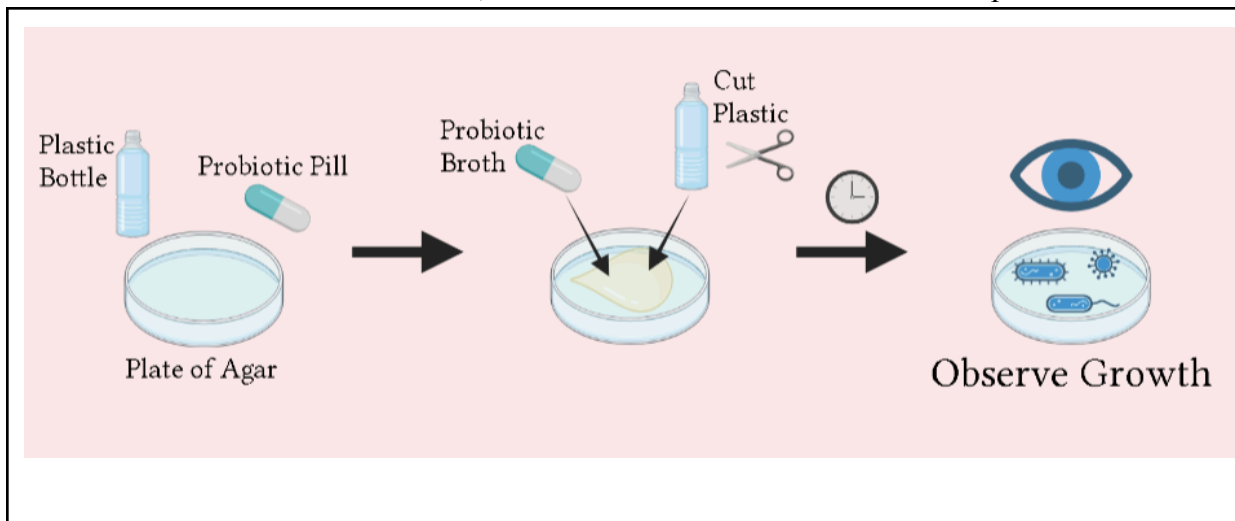
Fig. 4 Experimental design. Using two bacterial agar plates, one received 0.1g of microplastics while the other received 0.6g of microplastics (left). Next, we inoculated the two different plates mixed with a probiotic broth (middle). After a week on the windowsill at room temperature, bacterial growth is observed and documented (right).

The plastics were prepared ~1 wk. before we performed the experiment. We first poured the plastic in the plate, then poured the proper amount of agar to fulfill a mass of 10 grams of solution. We then allowed the agar to cool, while pouring two of the probiotic pills into a beaker containing approximately 25 milliliters of water. The swab stick was then placed within this mixture, and then streaked across the plates using a classic streaking method. They were then placed on the windshield at room temperature. Exactly a week later, we checked upon the plates to see the progress of the bacterial growth. We recorded any visual observations and took photos of each plate (Fig. 5).

A.

Area of Bacterial Growth experiment 1

B.
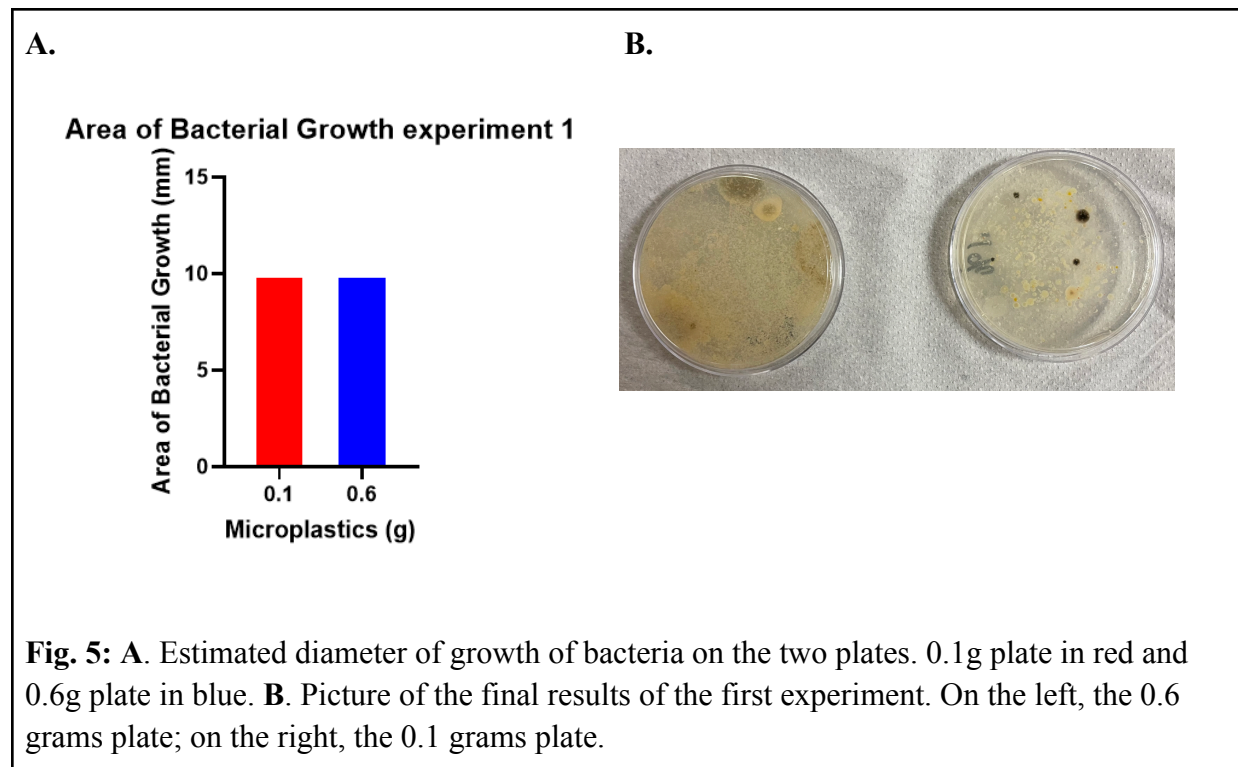
Fig. 5: A. Estimated diameter of growth of bacteria on the two plates. 0.1g plate in red and 0.6g plate in blue. **B**. Picture of the final results of the first experiment. On the left, the 0.6 grams plate; on the right, the 0.1 grams plate.

The results of the experiment showed that low amounts of microplastics, either 0.1g or 0.6g did not result in any significant changes in the spread of bacteria grown on the two plates. Yet, while the diameter of bacterial growth on the two plates was similar, the plate that had 0.6 grams of microplastics had bacterial colonies that appeared to be less dense than the one with 0.1 grams (Fig. 5 right).

We sought to repeat the experiment with a greater difference in plastic content. This time, while some parameters remained the same, others were changed to provide a stronger correlation

between the microplastics and bacterial growth. Two plates were prepared again, this time both contained 20 grams of agar solution. One plate was labeled the control group, and no microplastics were mixed within the agar solution. The other one was supplied with 1.8 grams of microplastics mixed within the agar. Just like before, the agar was given ample time to cool down before any further steps were taken. This time, only one probiotic pill was mixed within 30 milliliters of water. To each plate, 250 microliters of this probiotic broth was added and spread out across the plate surface. These plates were put in a cabinet within the room (at room temperature), and left to incubate for 24 hours. Upon examination, significantly more bacterial growth was seen on the control group with no microplastics than on the experimental plate with 1.8g microplastics (Fig. 6).

A.   **B.**
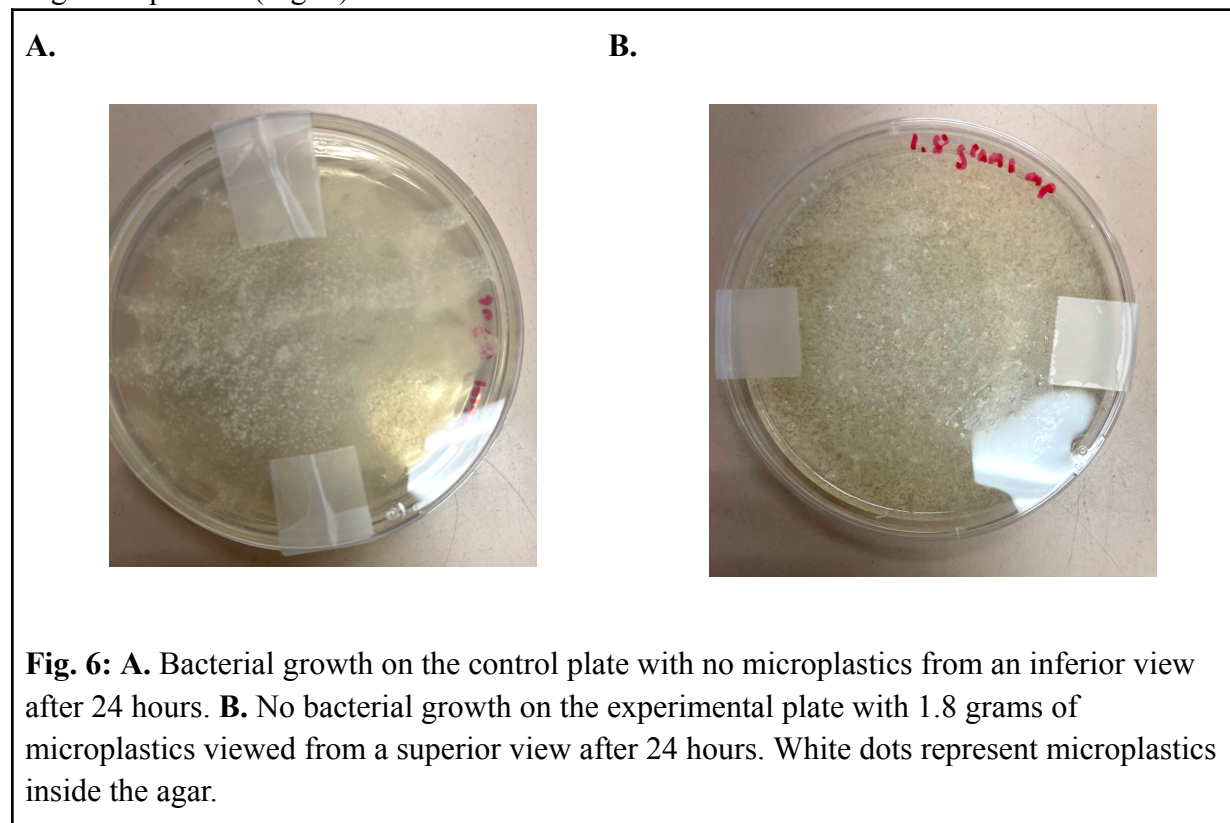
Fig. 6: A. Bacterial growth on the control plate with no microplastics from an inferior view after 24 hours. **B.** No bacterial growth on the experimental plate with 1.8 grams of microplastics viewed from a superior view after 24 hours. White dots represent microplastics inside the agar.

While *in vitro* results are limited by their exclusion of cellular components, the experiments completed here have shown a correlation between microplastics and bacterial growth (Fig. 5-6). The greater difference in microplastic volume between the two plates proved to also provide more significant and clear results (Fig. 6). In addition, we did not observe a wide variety of different species on the plates in experiment 2 compared to experiment 1. This may be due to the shorter incubation period, a parameter we chose to modify to observe initial microplastic inhibitions on bacterial growth. Still, the plate with the microplastics did have minimal growth, and even under view of a microscope no signs of bacterial colonies were found.

Discussion

        Through this study, we reviewed previously published data on the relationships between processed foods and the human gut microbiome as well as microplastics and the human gut microbiome. To accomplish this, we looked at large datasets of microbiome analyses from countries who had reported either low or high amounts of consumed processed foods or microplastics levels. While processed foods and microplastics are just two of the many environmental conditions that can affect microbiome homeostasis, we found it important to focus on these specifically as the amounts of consumed processed foods and inhaled microplastics are growing across the world.

        To combat these changes in microbiome levels and compositions and therefore restore one's normal microbiota, we predict that diets rich in whole grains and organic foods can fuel healthy bacteria and maintain healthy ratios between species. Avoiding higher levels of processed and high-fat foods helps decrease the high levels of unhealthy Firmicutes found commonly in the United States. Many of the common shifts in the microbiome can be attributed to personal dietary habits, but as the world increasingly becomes riddled with more and more processed foods, it becomes harder to avoid these causants. Similarly, as plastic production increases, it becomes harder to avoid contact with microplastics. Additionally, microplastics are so small many times contact with them is unknowing, further increasing the risk.

        In order to ensure the long term safety of the general public and their microbiome, action must be taken against unregulated production of microplastics and overconsumption of processed foods. Besides the environmental effects these products have, they also have been proven to have consequences on human health, specifically on the gut microbiota. Ensuring that levels of these hazardous materials don't increase is only the first form of protection against long lasting, widespread effects. In the case of established alteration of the gut microbiome, it would be wise to invest in probiotics and antibiotics to assist in reestablishing a strong, diverse community of bacteria. In cases where alterations of the immune system have the chance to lead into adverse health outcomes, providing available and affordable remedies for those problems in the form of pill or tablet supplements will reverse any detrimental and/or long-term effects.

Conclusion

        It is incredibly beneficial to have a healthy and diversified gut microbiome, both in the individual and the overall population. A healthy microbiome will be more resilient to any foods, antigens, or any other problems that arise within the human body. Having an entire country of people with healthy microbiomes ensures a healthier population, with lesser risk of gastrointestinal diseases and obesity, among other diseases. It is integral that studies continue to explore the correlation between microplastics, processed foods, and the microbiome. It might be especially interesting to look at correlations among all three. Seeing that general human health is on the line warrants a sort of public health response, as well as a reaction on the individual scale.

Limitations
- Lack of information on amount of microplastics in an agar that might restrict bacterial growth
- Limited materials led to small sample size
- Limited incubators at different temperatures
- Limited ability to experimentally test processed foods vs. microbiome due to human involvement and cost

Acknowledgements

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Should the SEC's Classification of Crypto-assets Fall Under the Same Category as Securities? By Divyansh Kumar

Introduction

After 2022, a rather unfortunate year for cryptocurrencies, the Securities and Exchange Commission has picked up a very aggressive approach towards their enforcement actions, especially against cryptocurrency exchanges. Owing to the rapid rise in the exchange of cryptocurrencies, the question of their legal classification has arisen. The SEC has recently taken action against well-known cryptocurrency exchanges such as Coinbase Global Inc. The SEC believes certain cryptocurrency exchanges, such as Coinbase, have been offering securities without registration with the Commission. Recent actions by the SEC beg the question: should cryptocurrencies be classified alongside regular securities?

Over the past decade, the use of cryptocurrencies has become more and more prevalent in day-to-day transactions. Cryptocurrencies have turned from being a neglected form of currency to a vital part of our financial world in an incredibly short time frame. Similar to any other vital currency, their legal classification is very significant as it allows the government to identify and better understand how they would like to regulate cryptocurrencies. The government currently considers a handful of cryptocurrencies as securities as per the SEC's ruling. This paper regards the government's classification of cryptocurrency assets alongside what is considered "normal" securities. It shows how irregular cryptos are in comparison to long-standing, traditional securities. This great irregularity and the large difference between the two show why a separate classification for them is necessary. The classification between the two is critical, as an "incorrect" classification of a cryptocurrency could greatly harm it and the large number of users that invest in the decentralized currency. Improperly regulating cryptocurrencies as securities could also bring a lot of unnecessary complexity to cryptocurrency investments.

This paper defines securities and cryptocurrencies and examines the differences between the two. It also shows why crypto-currencies should not be classified as securities and proposes an alternative classification structure for the SEC. Part I defines how securities came to be defined and provides examples of historical enforcement actions taken by the Securities and Exchange Commission. Part II outlines the rise and exponential increase in the use of cryptocurrencies and describes how Blockchain technology functions and the lack of unique alternatives. Part III highlights modern-day issues surrounding cryptos being classified as securities by providing examples of exchanges accused of offering securities. Part IV summarizes why the separate classification is necessary and provides an alternate classification structure.

This paper concludes by suggesting that cryptos should not be classified as securities and require a separate classification.

I. How Securities Came to Be Defined.

A. The Securities Exchange Act of 1934.

The Securities Exchange Act of 1934 was passed on June 6th, 1934 in order to address the stock market's opaqueness and lack of regulation. The Act was passed through Franklin D. Roosevelt in hopes of making the United State's market more fair and just to both investors and companies. Another outcome of the Act was to assist in reducing fraud and manipulation, both of which would contribute to the larger goal of making the market a fair environment.

With the passing of the Act, a new organization was formed that was responsible for working to meet the government's goals and standards. This organization was the Securities and Exchange Commission, also known as the SEC. The SEC was given the role of prosecuting any companies or individuals who break their policy. These activities are known as the SEC's enforcement actions. The SEC was split up into five different divisions, all with different tasks, including enforcement, economic risk analysis, and investment management. The passing of the Securities Exchange Act of 1934 was a necessity at the time due to the state of the US economy. Several factors necessitated the need for regulation in the market, with one major factor being the 1929 stock market crash. This 1929 crash began when the DOW Jones Industrial Average was down 20% through mid-1929, which caused considerable panic selling that continued for the remainder of the year.[1] The index did not return to its 1929 peak amount until 1954, making it one of the most significant bear markets in Wall Street history. *The Atlantic* describes investors at the time period: "...because of jobs, 'connections', the friendships that men curiously acquire with others of different ethical standards, or hopeless cynicism, these individuals do not dare or choose to be publicly critical."[1] This excerpt from the magazine shows the financial greed and irresponsibility investors displayed at the time. Flexner later describes the power of insider trading and notes how common it was. Financial corruption became yet another reason the regulation that the Securities Exchange Act of 1934 was needed as gravely as it was.

After the passing of the Securities Exchange Act of 1934, changes in the economy were immediately noticed. To this day, the SEC initiates enforcement actions against countless parties in hopes of creating a better economy for all investors and companies. Each year, the Commission investigates and prosecutes thousands of corrupt companies or individuals for violations, from failing to publish quarterly reports to insider trading. Although the SEC has been successful for the majority of its time running, there have been periods where they are not as powerful as the government wishes. An example of this is in the 1980s when some believed the SEC simply could not keep up with the financial lawlessness and the large number of bank failures.

B. Historical Enforcement Actions Taken By the SEC
The SEC has taken countless enforcement actions against many different companies. A select few of these enforcement actions were building blocks for the SEC and many of the future cases it may conduct. One landmark case that set a foundation for nearly all future cases regarding securities is SEC v. Howey Co. This case took place in 1946, involved a citrus grove in Florida. W.J Howey(owner of Howey Corporation) was selling investment contracts for his

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[1](Flexner n.d).

citrus grove as investment contracts to investors, many of which had no relation to agricultural means or farming. The investors would buy a portion of the land and lease it back to another company of Howey's. The citrus grove's workers would tend to the fruits and sell them as usual, and the investors would get their share of the revenue. The court determined that the land was an investment contract. This ruling created a precedent for countless cases, now commonly referred to as the Howey Test. Courts today use the Howey Test to determine if an asset is an investment contract. The test involves four different prongs: An investment of money, in common enterprise, has expectations of profit, and is to be derived from the efforts of others. This test has been a crucial aspect of determining whether a cryptocurrency is a security or not. The SEC has also taken numerous well-known enforcement actions against large companies such as:

- Wells Fargo: The SEC fined the banking company, Wells Fargo, $500 million for deceiving investors about their success. Wells Fargo was found to be opening fake, fraudulent accounts under their customer's names. The company also attempted to convince investors about their possible future success in a banking strategy they called cross-selling, where Wells Fargo sold customers products of Wells Fargo's choice.
- Tesla, Elon Musk: In 2018, the SEC charged Elon Musk with a securities fraud charge. Elon Musk claimed on the public communication app, Twitter, that he had the funding required to make Tesla a private company. This tweet caused the price of Tesla stock to increase by almost 6 percent, which the SEC believed was a "large market disruption". The SEC also found that Musk's tweet was not completely true, as he was not certain if he had enough funding. The SEC charged both Elon Musk and Tesla $20 million each and several changes in Tesla's structure, such as having Musk step down as Tesla's chairman and appointing new directors to the board.

Cases such as the Howey Test are used for almost all cases regarding the definition of security. This is important for the majority of cryptocurrency cases as if the SEC believes a cryptocurrency exchange is offering securities without registration, the exchange company or the prosecution can refer to cases such as the Howey Test to their advantage.

II. Traditional Types of Cryptocurrencies and Related Offerings
A. What is a "Typical Cryptocurrency"?

For the purposes of this paper, the term "typical crypto" defines the most basic form of cryptocurrency. This basic form is supported by the blockchain, is a digital asset, and contains a public, decentralized ledger. Additionally, the "typical crypto" is not a stablecoin, meaning that it is not linked to another asset such as gold or USD. Examples of "typical crypto" would include Bitcoin ("BTC"), Ethereum ("ETH"), and Binance Coin ("BNB").

B. The Rise and Exponential Increase in Use and Exchange of Cryptocurrencies.

Cryptocurrencies are a form of digital currency.[2] This currency can be used for numerous different tasks, such as for making payments or simply holding it as an asset. Cryptos are created

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[2] When referencing a "traditional" cryptocurrency it is referring to the most basic form of cryptocurrency.

by computers "mining" complex mathematical equations from the blockchain, a digital ledger. Control over a cryptocurrency's actions is decentralized and exercised by cryptocurrency users. Users also have access to a public ledger that records all of the transactions with a certain coin (this ledger does not directly connect to the identity of a person who used the crypto). Satoshi Nakamoto is credited as the inventor of cryptocurrency, although that name is a pseudonym, as the true creator was an anonymous programmer. Although Nakamoto was not the first person to conceive of the concept of a digital currency such as crypto, he created blockchain technology which helped in increasing the amount of digital currency available. This invention was a vital part of cryptos, something people considered the "final piece" of the puzzle.

Another problem solved by the ledger was double-spending. Since cryptocurrencies are not physical items such as cash, there was no way to detect someone spending twice using the same coin. Having a ledger that took note of all transactions was the solution to this problem. After the Financial Crisis of 2008, many people believed there needed to be a change to the traditional banking system. Having an online ledger that could be verified but not tampered with would remove any human error introduced by banking.

Over the past decade, there has been an exponential increase in the use of cryptocurrencies for all types of transactions. Certain sources, such as CNBC, use Daniel Polotsky's, CEO of CoinFlip, statement, which claims that cryptocurrency is "the best-performing asset of the decade, for sure". In the years of its existence, cryptocurrency has evolved tremendously. With this evolution, there has been a great increase in both the use and price of cryptocurrency. For example, Bitcoin's price has increased by thousands of percent during its years as a currency.

C. Staking and Other Types of Offerings

Cryptocurrency staking is a service where an individual holds cryptocurrencies and receives rewards for doing so by the exchange involved. When someone provides their cryptocurrency to an exchange it is usually in the form of a financial payment, that is later converted into a cryptocurrency. The "staker" is now holding cryptocurrencies in return for the rewards provided by the exchange. The cryptocurrency providers participate in the cryptocurrency's decentralized computer network. The cryptocurrency is used in the coin's blockchain to help validate transactions.

Although the service may seem appealing, there are a large number of risks that come along with participating in cryptocurrency staking. If the cryptocurrency being used is volatile, its price could decrease. If a staker were to receive a 20% yield, but the coin's price has dropped more than 20%, they are at a loss. Another risk involved with crypto-staking is the "holding" aspect. Certain exchanges require you to "lock up" your deposited cryptocurrency meaning you will not be able to un-stake it until a certain time period passes. This means if a cryptocurrency's price were to drop significantly while your cryptocurrency is locked, the staker is forced to take the loss. Hacking and fraudulent or insecure exchanges are also problems a staker has to be aware of.

Another offering similar to crypto staking is crypto lending. Crypto lending is the act of depositing cryptocurrencies to borrowers in return for compounded interest (in the form of the cryptocurrency lent). Cryptocurrency lending platforms are the "middlemen" who connect the lender to the borrower. Like crypto staking, crypto lending often has high return rates in the form of interest.

Similarly, DAOs are another cryptocurrency offering similar to cryptocurrency staking and cryptocurrency lending. Although not limited to only cryptocurrencies, the majority of DAOs are associated with cryptos and blockchain technology. A DAO is a decentralized autonomous organization that is operated by computer code. All members of DAOs use digital tokens to govern and control the organization. Members make decisions about the organization like investment strategies and funding projects such as software development. DAOs have many similarities to cryptocurrency staking services such as token importance, participation in governance, and autonomy. Problems arise with government regulation of DAOs as naming it as an investment contract is difficult due to characteristics such as lack of central authority and smart contracts involved with the organization. Other characteristics such as the token appreciation of members could be seen as an investment, provoking complex legal questions.

D. Differences between Staking and Traditional Cryptos

As discussed in previous sections, cryptocurrency staking is a risky investment that provides the opportunity for generous financial returns or severe losses. Cryptostaking and the use of traditional cryptocurrencies share a number of differences. When one purchases a cryptocurrency, they are holding an asset with the understanding that the value of their investment could change for better or for worse. Cryptocurrency stakers are expecting a set return within a certain percentage range of their initial amount staked. An additional example of a difference is another characteristic relating to an individual's intentions. Cryptocurrency stakers are staking their assets to be used for security and validity. Furthermore, cryptocurrency staking ideas such as the "lock-up" of currency is not present at all in the purchase and use of traditional cryptocurrencies.

III. Issues Surrounding Cryptos Being Classified As Securities

A. SEC Enforcement Actions: Cryptocurrency Exchanges Accused of Offering Securities

The Securities and Exchange Commission has recently taken numerous enforcement actions against different cryptocurrency exchanges with the belief they were selling securities without registration with the SEC. Examples of these include:

- Coinbase: On June 6th, 2023, the SEC charged Coinbase Global Inc. with the unregistered offer/sale of securities. Coinbase was also charged with failing to register its cryptocurrency assets in its staking-as-a-service program. The SEC claims Coinbase's operations are similar to an exchange, broker, and clearing agency. Due to this belief, they are being charged with operating without proper registration with the SEC. The lack of registration by Coinbase means that Coinbase did not uphold certain SEC regulations such as inspection and recordkeeping requirements. As Director of the SEC's Division of Enforcement, Gurbir S. Grewal said, "You simply can't ignore the rules because you

don't like them or because you'd prefer different ones"[3]. Coinbase was not charged with a fine as the Supreme Court sided with the cryptocurrency exchange and its claim that the definition of securities was not clear enough to prosecute Coinbase. Although the ruling was in Coinbases's favor, this may change in the future as the SEC has a number of paths it could take to reach its success.

- Binance: Shortly after taking action against Coinbase, the SEC also charged Binance Holdings Ltd with 13 different violations, many of which are similar to the charges against other cryptocurrency exchanges. Binance's charges vary from operating an unregistered exchange to misleading investors. For years, Binance has run different companies for investors in different regions. Cryptocurrency investors around the world would use the Binance website, while US investors had to use Binance US. This separation was put in place to help ensure US investors could use Binance while ensuring the company respects US legal standards. Part of the SEC's charges included accusations claiming that Binance was allowing high-value US investors to trade cryptocurrencies on their international platform, instead of being limited to the restrictions all other US-based investors faced. The SEC's misleading investors charges were based on their belief that Binance was lying to investors about market surveillance tools. The federal judge overseeing the case decided to decline the SEC's demand to freeze all of Binance US's assets and, suggested the parties agree on a conclusion that included mutually beneficial restrictions.

- Beaxy: Although certain charges against Beaxy Digital Ltd. were similar to the charges against other major cryptocurrency exchanges, the result was far different. The SEC found that Beaxy had raised large amounts of money, with the majority of it used for personal activities such as gambling. The SEC accused Beaxy of illegally raising $8 million through the unregistered offer BXY coin. $900,000 of the $8 million was supposedly used for the founder, Artak Hamazaspyan's personal expenditures. This is over 10% of the total amount raised. The SEC also found Beaxy had made an agreement with a financial services company, Braverock Investments. This Commission determined this agreement made Braverock Investments an unregistered dealer due to their assistance with Beaxy's market-making services. As a conclusion to the case, both Beaxy and the founder paid a fine and the cryptocurrency exchange was forced to close down.

A similarity noticed throughout these cases is the common charge of operating a securities exchange without registration. Although this is what the SEC believes these cryptocurrency exchanges are doing, this is not entirely fair as they are being tried as per the rules for traditional investments, not cryptocurrencies. Coinbase, Binance, and Beaxy are prime examples of this major conflict. Numerous cryptocurrency companies are being prosecuted and fined despite the SEC not having clear rules regarding cryptocurrencies and the sale of

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[3] "SEC Charges Coinbase for Operating As an Unregistered Securities Exchange, Broker and Clearing Agency." *U.S. Securities and Exchange Commission*, 6 Jun. 2023, www.sec.gov/news/press-release/2023-102. Accessed 30 Aug. 2023.

cryptocurrencies. Federal prosecution also sets a bad reputation for a company, further illustrating the necessity of proper cryptocurrency regulation.

Along with the damage inflicted upon cryptocurrency exchanges, the average consumer is also in jeopardy of being harmed. Without proper regulation, cryptocurrency investors will not be protected by the many laws of the government and the SEC that ensure market validity. The current lack of regulation and government involvement causes cryptocurrency investors to be at great risk of fraud, manipulation, and other forms of misconduct. Examples of this misconduct include the $1 billion worth of cryptocurrencies stolen from investors in just over 1 year and the 900% increase in cryptocurrency scams since March 2020.

B. Why Traditional Cryptocurrencies Should not be Classified as Securities

1. The Uniqueness of the Blockchain Technology and Lack of Alternatives

As mentioned earlier in the definition of cryptocurrencies, blockchain plays a key role in a crypto's success and ability to function. Its role in cryptocurrency is extremely unique and nothing similar to it is present in traditional securities, one of the many differences between the two.

Blockchain is a public ledger, accessible to everyone, and plays the main role in cryptocurrency. Certain characteristics of blockchain, such as its decentralization and publicity, makes it incomparable to securities. If cryptocurrencies and traditional securities were to be regulated together, the idea and purpose of blockchain could bring along lots of problems for the crypto. A decentralized ledger is something that attracts great amounts of cryptocurrency investors. If the cryptocurrency were regulated in a manner similar to securities, there is legitimate concern that this regulation would require centralized regulation and stringent adherence to unnecessary compliance laws.

Additionally, blockchain technology makes transactions much more accessible than securities transactions. This information is live and available 24/7. Currently, anyone is allowed to view and make transactions with a cryptocurrency through the technology of blockchain, as long as they have an internet connection. If security-like regulation were to come along, it could tamper with this accessibility which may be the "pulling" factor for some cryptocurrencies. A currency that is available anytime is very desirable, and cryptos are only able to do this due to blockchain. If cryptocurrencies were regulated the same as traditional securities, this increased regulation could remove the beneficial aspect of cryptocurrencies.

2. Traditional Cryptocurrencies Do Not Fit the Howey Test

As per the Howey Test, for an investment offering to be classified as an investment contract, it must meet all four characteristics that courts have used to define an investment contract. The four criteria of the Howey Test are an investment of money, an investment in a common enterprise, an investment with expectations of profit, and an investment that will be derived from the efforts of others. Cryptocurrencies as a whole do not fit into these standards as shown below:

- Investment of Money: Although certain cryptos are purchased through money, many do not agree with this rule as users have more than one way of obtaining a cryptocurrency.

Not only are cryptocurrency users able to purchase a cryptocurrency through normal money transactions, but users also have the ability to mine cryptocurrencies such as Bitcoin and Ethereum. Mining cryptocurrencies use computing power instead of a currency, meaning no money is directly invested into the cryptocurrency. Although certain cryptos may be bought "normally", a large portion of cryptos are obtained through mining. This means not all cryptos are an investment of money, so cryptocurrencies cannot be generalized into an investment contract with an investment of money.

- Expectation of Profit: Traditional stocks and securities are purchased with the sole expectation of profit from their investment. Cryptocurrencies such as utility tokens, are used to access a product or service using the same blockchain technology in all cryptocurrencies but the expectation of profit is not present with the use of these tokens.

- Common Enterprise: One of the most significant aspects of cryptocurrencies is their decentralized nature. For example, when purchasing a stock, the investor now has a very small ownership in the company. The stock they are purchasing is directly related to a publicly traded company that has a leadership structure with a CEO, head of departments, and employees. The success of the stock is based upon the success of the company. Cryptocurrencies do not have a set structure, and a great amount of stocks are completely controlled by the users of the crypto. Due to the decentralization, no one party is responsible for the success or the failure of the crypto.

- Efforts of Others: Cryptocurrencies like Bitcoin and many other cryptocurrencies's success are not based upon one entity. All users contribute to the cryptocurrency by mining or purchasing using a currency. Decentralized cryptos are often conducted as open projects and are driven by the technology that controls the cryptocurrency. Their success stems from all the users, not one specific third party as seen in traditional securities and stocks.

Overall, cryptocurrencies fail every prong of the Howey Test, and therefore should not be classified as investment contracts or fall under the same regulation of stocks and other market offerings regulated by the SEC. The analysis of the criteria makes a similarity evident between all prongs: The Howey Test's criteria is not applicable to all forms of cryptocurrencies, only certain types. Using a form of regulation that is not fit for the asset in question is the reason we face the regulation issues that we do such as the issues with the SEC prosecuting cryptocurrency companies for operating an unregistered exchange. Current cryptocurrency regulation generalizes cryptocurrency and only takes into account certain types of crypto. A proper classification would be applicable to all forms of crypto, requiring it to be separate from traditional investments.

IV. Alternative Classification Structure
A. The Need for Separate Classification Between Securities and Cryptocurrencies

Regulation prevents chaos from occurring in an environment and safeguards investors. The SEC's responsibility is to prevent this chaos and fraud in the US market. In recent times, the

SEC has greatly increased their charges against cryptocurrency exchanges. The main motive behind this is the belief that these cryptocurrency exchanges are selling securities without registration, making them an unregistered exchange which is worrying for the SEC as unregistered offerings may be fraudulent. Unlike traditional securities and stocks, types of cryptocurrency and their uses vary greatly. Having the standard security classification for cryptocurrencies is unsuitable and not fair to all cryptos due to how much they vary. The need for a separate classification is necessary.

B. An Alternative Classification Structure for Securities and Cryptocurrencies

Asset classes, an organization method used by financial advisors, is the perfect solution to the conflict. Asset classes categorize different assets into categories such as real estate, stocks, cash, and equity. Having an asset class for cryptocurrencies would be the ideal solution to the problem surrounding cryptos. If cryptocurrencies were to have their own asset class, along with NFTs and the majority of blockchain-related assets, legality issues around the sale and use of cryptocurrencies would be solved, as they would have a set of rules tailored to the unique behavior and structure of cryptocurrencies. When prosecuted for whatever charge it may be, the judge would use the regulations and rules related to the cryptocurrency asset class. This regulation would allow a separate classification of cryptocurrencies and securities while still being clear and detailed, unlike the current confusion surrounding their regulation. Clear and distinct regulations would better enable judges to apply the law in their rulings and prevent the government from bringing unjust actions against cryptocurrency exchanges and investors.

The Howey Test analysis shows that the current regulation for cryptocurrencies is applicable to some but not others. The proposed classification structure would take this into account and have separate classifications for "typical cryptos" and "special cryptos". The regulation would include specific laws that allow cryptocurrencies to keep their unique characteristics while still being properly regulated. Regulation would include aspects such as market integrity, user validation, and documentation for taxes. Market integrity would mean allowing government and regulatory bodies to have greater access to cryptocurrency exchanges to assist in detecting suspicious activity such as a sudden increase in a user's use of cryptocurrency or abnormally large transactions(in comparison to the user's average activity). User validation would ensure that users of a cryptocurrency are true users and not scams such as impersonation scams. Although the taxation of cryptocurrencies may not be a suitable option, cryptocurrency users should still be required to report their capital gains/losses to the government to help track users and their actions. The regulation for cryptocurrencies would differ for each type of crypto. It would depend on whether several factors are applicable to the cryptocurrency or not.

For identifying "typical cryptos", the framework could be the following:

- **Does it have a published white paper**: A white paper is a document published by an organization or non-profit that provides information about a service or product they provide or are planning to provide. Many different cryptocurrencies have white papers, and their publication can help the reader or possible investor

better understand the crypto. "Special tokens" such as utility tokens, which are meant to be used within certain platforms, do not need to display their information to the public as greatly as a "typical crypto" may have to. This appplies to specific "special cryptos" such as security tokens that represent ownership of an asset. This information about the ownership does not need to be available to the public, making a published white paper less of a necessity in comparison to other cryptos looking for investors.

- **Is the cryptocurrency not used as a store of value?**: An asset with a store of value is an asset with a value that cannot be depreciated. "Typical cryptos" are not used as a store of value, as investors who are seeking a profit obtain this profit through a change in the asset's value. Cryptocurrencies that are used as a store of value would not fall under the classification of a "typical crypto", as their set value shows how their purpose is not for making a profit.

If a cryptocurrency meets the provided prongs, it would be subject to the regulation previously provided such as market integrity, user validation, and documentation of use. This government intervention would help protect cryptocurrency investors while still allowing cryptocurrencies to keep their unique characteristics. If the cryptocurrency does not meet the prongs of "typical cryptos", they would be classified as "special cryptos" as their use is far more uncommon. "Special cryptos" would be regulated in a looser fashion as the risk surrounding the use of "special cryptos" is far less than the risk of "typical cryptocurrencies". Common examples of "special cryptos" are security or access tokens.

V. Conclusion

In recent months, the Securities and Exchange Commission's increase in enforcement actions brought flaws with regulation to light. The SEC has had an exponential increase in their actions towards cryptocurrency exchanges with the belief that they are offering securities without proper regulation by the government. Countless cases with large name exchanges such as Coinbase and Binance expose the flaws of the outdated regulatory system for assets. An analysis of different enforcement cases and the current regulatory test, the Howey Test, illustrates the main conflict with current cryptocurrency regulation.

The Howey Test was drafted to be used to determine whether an asset is an investment contract or not. Matching cryptocurrency's characteristics to the Howey Test shows that the test is only applicable to certain forms of cryptos. Regulation that does not correctly describe the asset it is regulating is extremely unjust as organizations being prosecuted have to face large fees and have their public image diminished. Cryptocurrency exchanges should not be charged for operating an unregistered exchange, as the rules being applied to their case do not adequately describe their asset.

Because of the misclassification and regulation of cryptos, an alternate classification for cryptos is desperately required. A successful regulation framework proposal isolates cryptocurrencies from other assets with the use of asset classes. The cryptocurrency asset class is

then split into two different sectors: "traditional crypto" and "special crypto" regulation. Traditional cryptocurrency regulation would be applied to cryptocurrencies that were used or are intended to be used in the most "standard" way possible: Blockchain involvement, decentralization, and a public ledger. Special crypto regulation and classification applies to cryptocurrencies that still utilize blockchain technology but whose main purpose is not to obtain a profit through the use of the cryptocurrency. Typical cryptocurrencies would be subject to more government regulation as the money of the investor is at stake. Having government intervention would also help lower fraud. Special cryptos would be subject to regulation that is not as strict as not as much of a risk is present in comparison to typical cryptos.

The cryptocurrency market is evolving at an exponential rate. Like any other asset, their regulation must be flawless to help ensure legal clarity when issues arise. The proposed classification helps meet the needs of cryptocurrency exchanges and cryptocurrency users. Crypto is here to stay, and its regulation should be just for such a vital asset in our economy.

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How has the deaf experience of music in the US shifted from the 1850s to the 1980s, specifically in relation to the debate over oralism and manualism? How is the musicality of said individuals perceived by the normative American society? By Cole Prawer

Introduction

To many people, deafness might seem like the ultimate antithesis of musicality; on the surface, the aural component of an activity based in sound seems inarguably essential for its enjoyment. However, aurality is not as closely linked to musicality as one may assume, and the very meaning of 'deafness' has changed throughout the ages, both in cultural and academic connotations. Studying these changes makes the relationship between music and deafness easier to understand, though societal recognition is not the end goal of most in the deaf community. The hard of hearing have been misunderstood throughout history— mostly in the form of hearing people speaking for the deaf community from the outside in—a scenario seen no more thematically than in the case of Alexander Graham Bell, the father of oralism. Interestingly, the extent of involvement by deaf people in the musical environment has fluctuated dramatically depending on the mode of communication in fashion at the time. Thus, a study of musicality and deaf culture must also include an account of linguistic history to fully represent the motivation behind cultural behavior. In the end, one can interpret sound waves as music without an aural component. Essentially, this paper seeks a resolution to the question of how the debate over oralism vs manualism of the 1850s to the late 1900s affected deaf culture, particularly in relation to deaf individuals' experiences surrounding music, and if the stories of the deafness of deaf musicians overshadowed the artistry of afflicted people. Ultimately, both manualism and oralism had ideologically corrupt foundations, which later morphed into more accepting (of musicality), positive versions of themselves in the 21st century. The real message is that the creation of multiple modes of communication helped in the long run by providing hard-of-hearing people the power of choice between linguistic systems in the 21st century, and debate between the two leading systems simply held progress at a standstill until resolved.

Section 1: Intro to Deafness—Definitions, Injustices, music, and Types of Disabilities
Section 1.1 – Defining Deafness

Deafness, throughout history, has had different definitions, and many might have misconceptions about the aural experiences of 'deaf individuals.' In reality, there are two main groups of hard-of-hearing individuals. The culturally deaf, and the non-culturally deaf. This is because many deaf individuals don't consider themselves disabled. Rather they are part of a linguistic minority. This makes sense when you consider that aurality is used as a means of communication most of the time. When a hearing person is in a room with a group of people who speak a different language, aren't they essentially 'deaf,' in the sense that they can't audibly discern what anyone is saying? The only difference between that anecdote and a deaf individual is that instead of speaking a different aural language, theirs is communicated via sign language (under the manualist model). Additionally, most deaf individuals don't hear 'nothing at all,' and

the differences in what they *can* hear varies. This starkly contrasts the stereotype of a hard-of-hearing person who can detect zero sound. While the standard for someone to be considered 'profoundly deaf,' is if one "...cannot 'hear' sound below ninety-one decibels," (Holmes 3) which is around the sound level of a leaf blower, it is important to note that "hearing thresholds vary according to frequency" (Holmes 6). The types of sounds a deaf person can hear are unique to them. In fact, 'residual hearing' isn't abnormal; "d/Deaf people seldom live in a world of absolute aural silence" (Holmes 6). This variation is what makes the definition of deafness so hard to get a scientific consensus on and has changed over the decades. Therefore, some hearing-impaired individuals relate to deaf culture (sign language + community outreach) while others don't. In this sense, there are culturally deaf people and other hard-of-hearing people who pass as hearing (Holmes, Quaglia). The individuality of deafness is truly astounding—it would be a disservice to lump the deaf experience into a definitive definition since:

> "There is no typical experience of deafness, and deaf people do not form a single, homogeneous social group. Rather, d/Deaf people relate to "deafness" in vastly different ways: deafness entails a combination of individual audiological characteristics, linguistic preferences, identity politics, and in some cases technological constraints" (Holmes 6).

All this being said, this paper will herein adopt some terminology that might conflict with the language used in prior research. Firstly, the terms used to address those afflicted with deafness will be 'hard of hearing,' and 'deaf individuals/people.' This is because those terms are most widely used in deaf communities, contrary to others like 'hearing impaired.' (That term might be used to refer to the loss of hearing itself, but not the person.) Additionally, since deafness is widely considered a disability by those experiencing it, this paper will refer to it as such even though there is much debate as to whether it falls under that category. Finally, when using the term 'deaf,' this paper will forego the usage of 'd/Deaf' notation, which is intended to provide a distinction between the hard of hearing and those who are 'culturally deaf' (because there are those who are hard of hearing, but not self-identifying with the culture). This notation is foregone because, in all contexts where the distinction might cause confusion, it will be made clear via plain text which group of people is being referenced. This will make it easier for the average reader to follow along with such a ubiquitous term in this field of study. (Holmes)

Section 1.2 – Different types of injustices

There is one more word that must be understood, and it has a few subtypes. These are the three types of epistemic injustice: testimonial, hermeneutical, and contributory, which contribute to normative societal disadvantages of deaf individuals. Epistemic injustice as a whole relates to injustices caused as a result of issues related to knowledge and one's access to giving and receiving it. Testimonial injustice is when someone isn't considered credible as a source of information. Hermeneutical injustice, the term most vital to this paper, is when a difference in a

group's shared experiences makes it hard to understand a member's conveyed knowledge. This second term is applicable to hard-of-hearing people when a subject that might be apparent to a hearing audience is foreign or unclear to them due to their disability and life experiences (Maler). In other words:

> "In the first type, testimonial injustice, a prejudice causes "a hearer to give a deflated level of credibility to a speaker's word"—in other words, the speaker is not seen as someone who gives credible knowledge. The second type, hermeneutical injustice, begins before an interaction, when some gap in our collective epistemic resources makes it difficult or impossible for a person to make sense of their experiences" (Maler 5).

The final type of injustice, contributory, results when "a perceiver [continues] to ignore the knowledge and experiences of marginalized knowers" (Maler 5). This version of epistemic injustice is not as necessary to understand this paper as the others. Additionally, it is with noting that 'epistemic injustice,' is a branch of 'epistemology,' which is the larger study of the theory of knowledge—specifically how it is shared and acquired (Maler).

These types of injustice build up one's place in society and affect who one is, how one acts, and what one knows. Thus, through these injustices, which are truly just limitations on giving and receiving information, the basis of all modes of communication has been born. Each seeks to remedy the injustices, but all for their own, sometimes misguided, goals.

Section 1.3 — definition of music

For the purpose of this paper, I propose the definition favored by aesthetics-focused philosopher, Jerrold Levinson, which stipulates that,

> "...music is 'sounds temporally organized by a person for the purpose of enriching or intensifying experience through active engagement (e.g., listening, dancing, performing) with the sounds regarded primarily, or in significant measures, as sounds'" (Davies 3).

There are a few key distinctions made in this definition. Firstly, because the sounds must be humanly produced, environmental aural elements such as birdsongs can be excluded (Davies). Some may disagree with this distinction, but for the sake of this analysis, this discrepancy hardly makes a difference. Remember that this section solely defines music to create a lens by which the rest of this paper can operate. Secondly, while the aural component is agreed to be the most common experience of music, this definition still leaves room for other interpretations. This subtlety is allowed by the latter half of the Levinson quote. The key distinction is that the main prerequisite for a sound being 'musical,' is that there must be intent on the behalf of the person creating it. In other words, as long as a person purposely creates sounds with the intent of "enriching or intensifying experience," (Davies 3) it can be considered to be music.

However, there is one large issue with the Levinston definition. Not all sounds that are widely considered music—again, one of the main attributes of music is its universal

recognizability—are, "not always intended to call attention to [themselves]" (Davies 3). Think of background accompaniment at an amusement park or a melody hummed under someone's breath. Neither wishes to command full attention, but most people would likely consider them to be music. In this sense, another distinction can be made. Levinson might allow these non-attention grabbing sounds to be, "quite properly called 'music' despite [their] lack of pretension to art status." In other words, a sound can be classified as music without the artistic attributes of music that meet the requirements of the Levinson definition.

At the same time, music exists both as an aesthetic object and as a cultural and community building activity. Instead of considering music to be a noun, it can also be understood through an analysis of the widely-encompassing *action* (verb) of 'musicking.' Christopher Small, the man who coined the term, and other academics/musicians interested in the study of musicology would assert that this approach might be a better way to handle the definition (Dell'Antonio).

But, what exactly does it mean? We often hear that one must not use the word one is defining in the definition itself. However, Christopher Small explains musicking as, "to take part in any capacity in a musical performance, and the meaning of musicking lies in the relationships that are established between the participants by the performance" (Small __). In essence, the action of, 'to music' lies not in the music itself, but in the performance. Thus, the musicality of said performance is actually not of the utmost importance—just that the musician has material to engage in a social event with an audience. Since Small claims that 'musicking' is a better way to define 'music,' he essentially relies on the fact that music can be universally recognized, and focuses on the social implications of the art as the defining feature it holds.

This new way of looking at what music is can be utilized well in the context of this paper because it bypasses the intricacies of having to prove each of the various modes of non-aural music meet the definition of music, by simply relying on the fact that if it is being performed, and can be recognized (usually universally) as being musical, then it meets the definition. One might ask what percentage of people have to come to the consensus that something is music before it can be agreed upon, but since the essence of musicking is mainly established by the "relationships… between the participants by the performance," (Small __) only aforesaid group of participants would have to agree on the musicality for each instance to be considered as such. Thus, when discussing sign-language rapping, only the active participants have to acknowledge, implicitly or explicitly, that musicking is taking place, for the criteria to be met. Future research, if prompted, could prove the musicality of each instance of deaf expression of music, but for our purposes, defining music as being a verb saves unnecessary complications while getting the same information across.

SECTION 2: Manualism vs Oralism (and resulting culture shifts in the deaf community)

Section 2.1 – Manualism

In the early to mid 19th century, manualism was the main teaching method for the deaf, and was created with the intention of bringing the Gospel to the deaf, and thus to establish their

'moral consciousness.' Manualism is "the practice of educating the deaf using sign language…" (Holmes 7) and was the mode of communication first introduced to the US deaf population.

> "Schools for deaf people were first established in the United States by Evangelical Protestant reformers during the Second Great Awakening… The first school, the American Asylum for the Deaf and Dumb at Hartford, Connecticut, was founded in 1817 by the Reverend Thomas H. Gallaudet, with a young deaf man from Paris, Laurent Clerc, as his head teacher" (Baynton 3).

Not that in this context, the term 'dumb,' refers to an inability, or unwillingness to speak—it is not used to degrade intelligence. With the creation of this school, along with others that soon followed, a community of hard-of-hearing individuals began to form with numbers that were larger than ever before. In the 1800s, deaf individuals might go for most of their lives without meeting someone with similar experiences, so this new community was a force for self-acceptance, and—since many of the students were in adolescence (Baynton)—a good environment for moving into adulthood. Moreover, early schools for the deaf were helpful in terms of their actual curriculum; many students learned, "for the first time, how to communicate beyond the level of pantomime and gesture" (Baynton 3). There is no denying that this institution had a positive impact on many hard-of-hearing people. Still, there were quite a few faults.

In the Christian community, deafness was considered to be a blessing in some cases, as it preserved the 'innocence' of a person to a degree, or so they claimed. Theoretically, they couldn't hear impure rhetoric and were less tainted by people who would have been considered sinners. On a darker note, since they thought that religion was the path to basic morals, they considered deaf individuals to be almost animalistic until they learned to communicate with sign language and learn the word of the gospel. The specific problem that they had with deaf individuals was that they thought they, "lived beyond the reach of the gospel. They knew nothing of God… nor had… a firm basis for the development of a moral sense" (Baynton 8). This meant that their motivation for giving a means of communication to the deaf was not based on helping them for the sake of doing good; they simply wanted to spread Christianity. The deaf population being able to speak to others wasn't on their minds at all; they had their own agenda. This marks that there are, in fact, issues with the origins of the manualist system. In the following paragraphs, one might derive that oralism is the only mode of communication with negative ideological roots, but this is untrue.

Though it was born with an ideology that dehumanized the hearing-impaired population, this mode of linguistics, as aforesaid, has historically been beneficial, giving the deaf their own culture, and proposing the idea that 'normal' hearing isn't the end all be all of the human experience surrounding sound. Manualism tried to promote Christianity, but it didn't force deaf people into assimilation and misguided hopes of being 'normal'—if 'normal' has a real definition—in the same way that later systems would attempt to. The deaf don't need to pass as 'hearing.' They can challenge what it means to communicate effectively and deeply in the first

place. (Holmes) It is worth noting that in the modern day, teaching using sign language has little to do with Christianity, and it is simply a mode of communication. Thus, the hidden agenda has been taken out of the manualist form of education, making it an appealing contemporary format. Additionally, since manualism was only born for the purpose of learning the gospel, the physical act of sign language was actually quite arbitrary for its original intended purpose, and the founders could have chosen any other mode instead. This goes to say that the manualist system could have very well used lip reading (like oralism)—had the original schools chosen it—since the reason for its invention was solely based on giving the deaf a means of learning the word of God. Thus, understanding the ideologies behind it is more important than the specifics of signing, or the people who designed it.

Section 2.2 – Oralism

As aforesaid, in the 1860s, deafness was considered to exclude a person from 'the reach of the gospel.' Thus it was heavily looked down upon. After that, about a decade later, deafness was no longer a problem against Christianity, but that it cut people off from English, and thus larger American culture. From this, oralism, a method that teaches the exclusive use of speech and lip reading… coinciding with the height of the eugenics movement…" (Holmes 7) was born. With it, the linguistic form, grandfathered by Alexander Graham Bell, "… sought to eradicate a then emerging subaltern deaf culture by suppressing sign language use with the aim of assimilating the deaf into hearing culture" (Holmes 7). The fear that the eugenics-fused proponents of oralism had was that sign language encouraged the deaf population to create their own culture and life secluded from the rest of the broader American society. Thus, Bell and his associates were afraid of the creation of an entirely deaf version of the human race. If that sounds like the theory is in favor of eugenics, limiting the breeding of deaf individuals, that is because it very much was. Parallels to Nazi Germany and the paranoia against disabilities can certainly be drawn. With the invention of this system, the battle between oralism and manualism was on, and "tensions… fostered two sharply divided approaches to deaf language use and identity, a pedagogical "war" that… persisted until the late twentieth century" (Holmes 7). Even with such a divide and controversy—, due to its appeal to hearing parents, who were hopeful that their hard-of-hearing children could assimilate, and its apparent cost saving by the state department, oralism completely dominated manualism until the 1970s. It had the promise of breaking deaf people out of the supposed 'confines' of their hard-of-hearing communities and thus came with a certain social appeal. Schools were forced to stop teaching manualism, punishments were put in place for signing, and a sharp stigma was placed on deaf individuals who couldn't learn to lip read (which had a lengthy learning process). Deafness had its communication medium changed over time according to whom educators deemed as an essential community. Both oralists and manualists portrayed deaf people as outsiders, they simply differed in who they wanted them to align with. According to oralists, the group that deaf people had to fit into was the general society, and for manualists, it was largely the Christian community. (Holmes)

SECTION 3: Hearing-impaired individuals' relationship with music, and the over-romanticization of disability, specifically in the manualist movement

Section 3.1 – Music and Disability Studies

Music is much more of a multi-sensory experience than it is often given credit for, and every person with hearing impairments has their own unique way of engaging with it. Deaf individuals not only interact with music through their purchasing power, but directly contribute to it as musicians. "'[T]he canon of Western classical composers is not diverse with respect to race, class or gender ... it is with regard to disability.'" (Quaglia 15, Straus) Famous examples such as Beethoven and (the contemporary) Evelyn Glennie strike out in this field, but they are far from alone. Since deafness has such a wide-ranging definition, different people relate to it in entirely different ways. And, this isn't a novel idea since, "[d]isability has played a central role in Western art, from its origins in classical antiquity up to the present time" (Straus 64). Looking through history, a surprising number of musicians have been hearing impaired, and "[d]isability has been hiding in plain sight…" (Straus 64) for a long time. It is also important to note that while vibrations—as in the physical presence of sound waves through air and solid mediums—are a large part of the deaf experience of music, they are far from the only one. Sign language rapping, for example, "...enjoy widespread popularity within the Deaf community" (Holmes 23). Additionally, not everyone in the deaf community agrees about their relationship with music, and some might think that it doesn't relate to them at all. It all comes down to personal preference and situation. In Western culture, starting from the 1850s, the closer to present day, the more open-minded society has been to deaf individuals choosing their own path without outside intervention from people like Alexander Graham Bell and other 'deaf educators.'

Section 3.2 – Oralism and Manualism's Beliefs on Deaf Musicality

The oralist movement, in the beginning, used music quite frequently. However, in their eyes, it was simply a tool for assimilation. If the deaf could sing, they could blend in with the hearing population all the better. They encouraged participation in the activity until "…the second half of the century [when] they became increasingly suspicious that deaf music making was mechanical and morally corrupt…" (Holmes 22) since they couldn't hear what they were playing. They believed that the deaf were creating music like robots since they couldn't aurally experience it for themselves, and thus reasoned that their skill must have been based on rules and clearly defined melodies, making the process uncreative and illegitimate. The oralists didn't understand what modern disability studies have learned about the extent to which music can be understood without aural perception. This comes back to hermeneutical injustice; since the hearing oralists couldn't understand the deaf musicians' experiences, the knowledge shared by said deaf musicians was discounted. So, by not fitting the norm, their opinions were kept out of the pooling of knowledge. Just like the rest of life, hearing isn't black and white. With each different person comes a new experience with sound, meaning that one cannot generalize the deaf experience. Music *can* and *is* enjoyed by the hard-of-hearing. (Maler)

The manualism movement, on the other hand, didn't have much to say about musical participation other than being used as a means of teaching non-aural perception of sound. Since they only cared about the deaf population learning the gospel, they left it up to the individual to

either opt-in or out of the activity (music is defined as an activity under the 'musicking' definition). This made music more accessible than the oralist movement—after they considered music a taboo—but they didn't encourage active participation, and more so just 'let it happen.' In the modern age, both forms of education openly promote musical participation, but many deaf individuals make the choice not to take part in the field for a number of reasons. Firstly, they might feel that music *is,* after all, dependent on aurality. Even though this paper disagrees with this premise, every deaf person has a right to their own opinion. It is worth noting, however, that there are also a large number of people who feel they *do* have a part to play in the realm of musicality. For examples of such people, visit 'Section 4.'

Section 3.3 – Over-Romanticization

Though overcoming hardship is certainly admirable, it is important that the hardship itself doesn't take precedence over the fruits of one's labor. Classically, incredible musical ability, or any special ability for that matter, has been considered as 'compensation,' for impairment. They believed that divinity had taken one sense in exchange for a gift. Additionally, whenever a deaf musician makes/made headlines, their condition almost always precedes their actual accomplishments. Their success is seen as a win *despite* their circumstances, making their disability take center stage over themselves. The act of this can reduce an individual to a condition and limit the acclaim of their actual creations. However, at the same time, one cannot deny the fact that disability can actually be a positive force in the musical creation process. It is inherently part of the work, and shouldn't be shunned. This harms the musician and society (by not giving the means of creation any attention); unfortunately, this happens all too much, with, "[t]he trope of disability heroically overcome is used as a primary strategy for focusing attention upon the music itself, and away from the disability," (Quaglia 4) minimizing an important aspect of the creation of the work. Like the careful chisel on marble, the artist, their circumstances, and their environment are all part of their productions. Still, as aforementioned, it is a thin line to walk, since one must not give disability *too much* attention either. Like all aspects of art, disabilities are simply one component of the final creation, and should be regarded as such—relevant, but not overpowering in the attention they are given. However, this is an entirely different subject than theories of divine compensation, as those can be harmful in framing disabilities as inherent punishments and payments. This line of thinking can lead to the stigmatization of impairment, which is always a negative ideology to subscribe to.

SECTION 4: Modern and contemporary deaf musicians and listeners

Section 4.1 — Contemporary Deaf Musicians

When picturing the deaf musician, Beethoven might be the only example apparent to most hearing individuals. Indeed, Beethoven did become deaf around his thirties, only to write his most famous work: 'Symphony No. 9.' Such a story deserves recognition, though, as mentioned in 'Section 3.3,' one mustn't let his deafness overcome recognition for the splendor of his work. With the advent of the modern concert, deaf musicians have more opportunities than ever before. Native signers, for example, have developed a new way of appreciating music in a

"musico-poetic expression" (Holmes 22) that follows a "'rhythmical cadence.'" In this cadence, signing is not just used as a translation for the deaf, but becomes incorporated into the song itself. In the same way that many songs would be more difficult (though very possible) to interpret without an aural component, these songs would be just as difficult to understand without a signer performing them. Indeed,

> "[in] the hands of native signers, in particular, song signing performances exceed mere translation where the visual-spatial contours of ASL shed new light on the musical and poetic dimensions of the song, transgressing the conventional structural demarcation of verse and chorus. Sign language rappers such as Sean Forbes and Signmark, all-deaf bands such as Beethoven's Nightmare, and other musicians belonging to D-PAN (Deaf Professional Arts Network) also enjoy widespread popularity within the Deaf community" (Holmes 23).

In the hands of deaf performers, visuality supersedes aurality altogether. However, this need not be the case; it is solely up to the musician. One deaf artist who opts to use sound is Evelyn Glennie, who focuses on vibrations through her technique of "'touching the sound'" (Holmes 2) as the first full-time solo percussionist in the world (PAS). Glennie might just be the most prominent contemporary deaf musician, having had "... the honour of a leading role in the Opening Ceremony of the London 2012 Olympic Games… [and] over 90 international awards to date, including the Polar Music Prize and the Companion of Honour…" (University of London). Glennie has also won one oscar and has been nominated for two more (Fellows 2). She focuses on percussion instruments and only developed her interest in the field until *after* she became fully deaf by the age of twelve (Fellows 2).

Interestingly, Glennie does not choose to associate with the deaf community, and has "long resisted self identifying as "deaf" or "disabled," in an effort to dissociate from the politics of deaf identity and the stereotypes disability begets, and ultimately to highlight the critical merit of her musical achievements over the seeming novelty of her deafness" (Holmes 3). She recognizes that the over-romanticization of 'overcoming hardship' can, at times, overshadow her actual work, and has decided to not let such a situation occur. Instead, Glennie considers herself to be a musician with a hearing impairment (PAS). Embracing the physicality of sound, "she performs barefoot (or in stocking feet), [and] "hears" the vibrations through her body" (PAS). Glennie has also "...invited audience members to explore their physical connection to sound by using their hands to create the sounds and sensations associated with different meteorological phenomena," to prove that, "sound is more than meets the ear; it is a multisensory experience" (Holmes 2).

Section 4.2 — Accessibility for Deaf Listeners

There are two main types of use cases of sign language (in the context of music) in modern culture. Firstly, the sign language interpreter. This is "a certified professional, trained to

facilitate communication between hearing, deaf, and hard of hearing individuals, often using American Sign Language (ASL) or Signed English." (NECC) The other case where sign language is used in music is by the artist themselves. In other words, not by an interpreter, but as a *primary* delivery mode of music. In the most recent Superbowl, deaf rappers Sean Forbes and Warren 'Wawa' Snipe performed, alongside a superstar cast, in sign language (Long). It is important to note that in that specific case, the artists were brought in as interpreters, but the key takeaway is that they additionally make their own music and are getting overdue mainstream attention. For the purpose of this paper, the former use of sign language will be discussed here but refer to section 4.1 for further explanation. This is because it is much more common for sign language to be used to interpret conventional music, and thus is a more popular gateway for the hard of hearing to gain access to the world of musicality.

Contrary to popular belief, learning sign language on its own does not automatically certify someone to be an interpreter. There is additional training required, and after getting approved, they might appear on the corner of a televised press conference, briefing, or at a concert, signing rapidly for the benefit of the hard-of-hearing. Despite the rise of ASL (American Sign Language) during the pandemic (Edwards), there is a current shortage of interpreters with a 50-1 ratio of sign-language users in America to certified interpreters (DSU). Still, the U.S. Bureau of Labor and Statistics reports that, "employment for interpreters is expected to grow by 20 percent by 2029" (Edwards). This implies that the shortage will not be indefinite.

Modern technology has helped the spread of sign interpretation since the primary use case is on television, but there are many other subtle technological advantages that might not come to mind immediately. Firstly, improved lighting systems make the deaf concertgoing experience easier, due to a clearer line of sight to signing friends and interpreters. In many cases, the deaf have an easier time communicating at especially loud concerts because sign language and lip reading aren't impeded by 'deafeningly' high volumes, while normal speech is. Additionally, a longstanding trend in many genres is to bass boost speakers, which makes feeling vibrations in the air all the easier. All this, coupled with handheld props, streamers on speakers, and other tactile feedback devices has made live shows much more accessible for deaf listeners in recent years (Holmes).

This subject lends itself well to displaying the usefulness of the combination of oralism and manualism, dependent on personal preference. While at a concert with close proximity to the performer, one might opt to lip read and feel the vibrations in the air; if situated far away from the performer, one might choose to look at the interpreter instead. But, the quintessential deaf concertgoing experience comes when a performance has good visibility of the performer, a loud bass line, and sufficient enough lighting to see both the dancers, the mouth of the artist, and the signing of other concertgoers for easy communication. Under this circumstance, it is up to the individual what to pay attention to: lip reading the musician, the interpreter, the vibrations, or their friends. Hence, manualism and oralism work in tandem to create a holistic environment. This gives the greatest power of choice to deaf music participants without creating a clash between differing systems. It seems that the century-long debate between oralism and manualism

was entirely unnecessary and better left to the preference of the individual. Communication truly becomes easiest when sign language and lip reading are married. Still, if a deaf person chooses to forego either mode, that should be left to their best judgment.

Conclusion

Historically, different linguistic theories such as manualism and oralism have incorporated implicit biases and hidden agendas. These philosophies based the standard on *whom* the general population wanted the deaf to associate with. They were never designed to help the people using them; in many cases, they were actively harmful. After the fierce clash of competing linguistic education models, both major methods became different options, corresponding with how deaf people choose to live their life—society no longer forces one over the other in a day and age that promotes inclusivity and diversity more than it has in the past. Still, there are situations where one system would make more sense over the other. There is also still substantial anger toward the oralist system and the assimilative tactics it has historically employed—causing some people to (understandably) never use it. Still, the democratizing of communication has led to manualism and oralism being run, for the first time, by the people employing it. In the modern age, therefore, neither system is superior to the other; personal preference dictates which mode one aligns with. As is the case with all different backgrounds of people, the hard-of-hearing have valuable contributions to make in all fields, musical or otherwise—not just because of their disability, but because of their innate human curiosity and self-expression. Today, in many cases, hard-of-hearing people have the choice of when, why, and how much they want to associate with deaf culture, and whether or not they want music to be part of their lived experiences—all in a way that is unique to them. (Holmes, Baynton)

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The Human Body By Seokjun Yoon

The human body is an embodiment of thousands of different bacteria, each of them having their own unique functions. For this review, we will mainly focus on probiotic and commensal bacteria. Commensal bacteria are a group of bacteria living inside the small intestine that aids the efficient performance of the small intestine regarding the absorption of nutrients. Probiotics are bacterias we consume in hopes of forming a mutual relationship with commensal bacteria. Because the probiotic bacteria share the same function with commensal bacteria regarding the support given in digestion, probiotic bacteria sometimes give support to the commensal bacteria, increasing the efficiency of the small intestine. Despite its widespread benefits, developers of probiotic supplements still struggle to overcome probiotic bacteria's vulnerability in the journey to the small intestine, which is caused by extreme temperature and moisture fluctuations(Smith 4). The main issue with current probiotics is that not many bacterias actually reach the small intestine, and many probiotic bacterias die in the stomach acid. However, genetic engineering could be a solution to the problem, as altering the genetic makeup of the probiotic bacteria to increase in its chance of survival during its interaction with stomach acid may lead to a positive result.

Despite probiotic's well-known efficiency in enhancing our body's overall digestion, there are still major obstacles to overcome. The problem can be summarized into two categories: method of preservation and survivability.

Firstly, methods of preservation have always been a source of difficulty for scientists. The most effective existing solutions are encapsulation and freeze-drying(lyophilization). Encapsulated pills are primarily designed to prevent the exposure of moisture and stomach acid from altering the microbiological condition of the probiotic bacteria. However, when the encapsulated pills contact stomach acid, most of them melt away due to the low pH level of stomach acid. Probiotic bacterias sometimes die before they make contact with stomach acid due to the high level of moisture present in the stomach. Scientists could increase the resistance of the pill to make it completely resistant but cannot take initiative, as the increase in resistance would make the pill indigestible. Moving onto the freeze-drying process, this process has higher vulnerability to stomach acid compared to encapsulated pills. Freeze drying is the process of quickly freezing a probiotic bacteria at a temperature between -40 and -70 degrees celsius then evaporating the remaining moisture. Because the probiotic bacteria was rapidly frozen, it is extremely vulnerable to rapid temperature changes such as heat or humidity. The stomach acid has a high temperature of 37 degrees celsius, indicating that freeze-dried bacteria would instantly die after an interaction with the stomach acid. Due to this characteristic of the stomach acid, very few bacterias survive the stomach acid and go to the small intestine.

Secondly, there is no guarantee that a probiotic bacteria has a high level of survivability regarding the existing bacterias in the small intestine. Bifidobacteria is a bacteria that is commonly found in the small intestine that serves a similar function to probiotic bacteria, as it primarily aids the small intestine in digestion(Callaghan et al.). Because it performs a similar

function to probiotic bacteria, fights for colonization often happen between probiotic bacteria and bifidobacteria. The outcome of the fight mostly results in bifidobacteria colonizing over the probiotic bacteria through initiating a defense mechanism called "diarrhea, as there are possibilities which bifidobacteria considers probiotic bacteria as an intruder. Even if probiotic bacterias managed to fully colonize the small intestine, they have a limited function compared to bifidobacteria, making it unsure whether probiotic bacterias have the capacity to take on the responsibility of bifidobacteria's role. In fact, problems also lie in the probiotic bacteria's characteristics. The probiotic bacteria normally does not form colonies, meaning that it is mostly the individual cell of probiotic bacteria that has the responsibility of colonizing the small intestine. Another problem is that probiotic bacteria have a round, oval shape that is not fit for adaptation in the small intestine. Compared to probiotic bacteria, bifidobacteria has multiple pili (thin strands attached to the bacteria) that enables it to attach itself to epithelial cells that consist of the inner layer of the small intestine, increasing its rate of survival and enabling it to perform different functions.

Although there are many existing problems regarding probiotic bacteria, there are numerous innovative alternatives that could be implemented in solving the current problem. In order to discuss the alternatives, knowing about the factor that increases the survival rate of probiotic bacteria is crucial. Certain probiotic bacterias survive in the small intestine due to a lack of bifidobacteria. The lack of bifidobacteria reflects the increase in the amount of maintenance in the small intestine, which probiotic bacteria acts as an alternative to substitute bifidobacteria's role. Despite the fact that probiotic bacterias do succeed in colonizing the small intestine, the chances of it happening are very rare, which highlights the importance of genetic engineering to act as a good alternative in solving the problem.

Genetic engineering is a process that uses laboratory based technologies to alter the DNA make-up of an organism. Specifically, it is the artificial manipulation, modification, and recombination of mainly DNA or other nucleic molecules in order to modify an organism or a population of organisms. Like genetic engineering, most recombinant DNA technology involves the insertion of foreign genes into strains of bacteria. Once this inserted gene starts to work, the modified bacteria will produce the enzymes or proteins commanded by the foreign DNA. Due to the numerous possibilities the concept of "gene alteration" has, it is implemented in various different branches of science, from agriculture, to medicine. The food industry has been utilizing two main methods: 1)agrobacterium tumefaciens method, 2) particle gun method for genetic engineering("What is genetic modification (GM) of crops and how is it done?"). Firstly, the Agrobacterium tumefaciens method utilizes the characteristics of agrobacterium tumefaciens bacteria for genetic engineering. Agrobacterium tumefaciens is a soil microbe that infects its host through transferring a portion of its own DNA into the plant cell("Methods and Mechanisms for Genetic Manipulation of Plants, Animals, and Microorganisms"). The plant then reads and expresses the transferred genes as if they were part of its own cells. For genetic engineering, scientists replace the disease-causing DNA inside of agrobacterium tumefaciens with the desired DNA so that the plant expresses the desired DNA as it grows. Secondly, the particle gun method

bombards plant pieces with metal particles coated with DNA encoding desired genes(Kikkert 1). The DNA elutes off the particles lodged inside the plant cells and a portion of the DNA eventually combines with the chromosomes(Kikkert 1).

Amongst the different branches of science genetic engineering is closely intervened with, it has an extremely close relationship with microbiology(Liu et al.). Because of the close-relatedness with microbiology, its implementation on probiotics, a well known branch of microbiology, will be groundbreaking. Stomach acid and temperature fluctuations are features of the stomach that cannot be changed with application of technology, which highlights the need for a change in the bacteria itself to withstand the stomach acid and temperature fluctuations. With the help of genetic engineering, the problems with probiotic bacteria could be solved through making probiotic bacteria to have a similar function to existing commensal bacteria in our gut, such as helicobacter. Helicobacter survives the stomach acid by a mechanism called cytoplasmic urease(Liu et.al). It is a reaction in which helicobacter produces ammonia, a substance that is known to neutralize the pH level of the stomach acid, thus contributing to its survival. If probiotic bacteria could obtain the same characteristic as helicobacter through genetic engineering, its inability to survive in the stomach could also be improved, which will become a leading factor in the advancement of probiotics.

Another issue that genetic engineering could tackle is probiotic bacteria's survivability in the small intestine. Small intestine is mainly composed of bifidobacteria that carry out numerous functions to help maintain/improve its efficiency. Here, genetic engineering could be applied to make the physical features of probiotic bacteria to be similar to bifidobacteria or enable similar functions to bifidobacteria as a means in solving the current problem, and so that probiotic species do not trigger a strong immune response. One of the functions of our small intestine is to prevent infection, and one way it does this is blocking out the intruders in the form of diarrhea. It is our body's way of quickly clearing viruses, bacteria, or toxins from the digestive tract. Probiotic bacteria's relation to diarrhea lies in its production of short-chain fatty acid(Berger). An abundance of fatty acid can result in temporary diarrhea. Therefore, we can also engineer the probiotic bacteria through limiting its production rate of short-chain fatty acid in order to prevent diarrhea from happening.

Conclusion

Probiotic bacteria, a bacteria that is commonly known to many of us, can experience an increase in its productivity through application of genetic engineering. Genetic engineering provides many alternatives in probiotic bacteria's weakness, which are stomach acid and temperature.

In fact, genetic engineering is a field that should not be overlooked, as it can serve as a key in unlocking various conundrums that may seem unsolvable at this moment. Its possibility as a solution to many conundrums is highlighted in its adaptability to many different fields. Agriculture is a prime example of the field, as it has greatly benefited from genetic engineering due to the technology changing the genetic structure of crops, making it more resistant to pests

and ultimately increasing its size. The benefits of genetic engineering in the food industry is vast , genetic engineering is seen to have a large effect in the food industry due to its ability to add new DNA compositions to numerous foods. In fact, humanity is living in an era where biotechnology is increasing in importance, as global warming continues to alter the lifestyle and ultimately our bodily composition, as it continues to adapt to the irregular intervals of extreme weather. As global warming continues, genetic alteration is predicted to be an essential factor in ensuring adaptability to those harsh conditions. The same concept applies to our food sources and various organisms that constitute the environment we live in as well. Thus, although the future is unclear, it is evident that the value of genetic engineering is increasing and will continue to in the future.

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Do ESG companies in Saudi Arabia outperform market risk factors? Empirical Evidence from the Tadawul Exchange By Abdulrahman Ibrahim Alrajhi

Abstract

Environmental, Social and Governance (ESG) is an approach aimed at increasing sustainability and promoting ethical and responsible practices. Although it is yet to be mandatory in Saudi Arabia and is still in its early stages, this has resulted in ignorance of ESG, as the benefit remains unclear. In 2021 Murad Ali did a study on ESG reporting in Saudi Arabia and found that there is a significant gap in ESG reporting in Saudi Arabia, indicating that ESG in Saudi Arabia may not be mature enough to be considered. Additionally, a 2020 research paper by Hussein Mohammad Salameh that used the 5-factor model, 3-factor model and CAPM concluded that due to the nature of the Tadawul exchange being different to the rest of the world due to Islamic Sharia and laws, it is challenging to find accurate results. This research paper aims to run a linear regression using the Carhart Four Factor Model to five portfolios that consist of the top 50 ESG firms in the Saudi Arabia Stock Exchange (Tadawul) to uncover if firms more aligned with ESG are outperforming market risk factors. Empirically, the results show that the top 20 ESG firms in Saudi Arabia outperform market risk factors on a consistent basis; more specifically, the p-value rejects the null hypothesis, which indicates ESG outperforming regular stocks on a risk-adjusted basis, with the rest accepting the null hypothesis. The results suggest that while ESG is still a new topic in the business world, firms that are implementing it may benefit in the Tadawul Exchange. It is worth noting that the majority of the firms in the highest-rated portfolio were banks and telecom firms, which could invalidate the result. Further research is necessary to conclude the impact of ESG on returns.

Introduction

Can ESG be a viable investment metric? This is a question that recently has gained global relevance. With new government regulations and customer expectations that force businesses to align with ESG objectives, businesses in Saudi Arabia have seen increased pressure to improve their ESG awareness and implementation. With ESG in its early stages in Saudi Arabia, it is not yet mandatory across businesses and lacks awareness among stakeholders. This has resulted in poor ESG integration across many companies.

The increased pressure in Saudi Arabia to improve ESG in businesses was partially started by the Stock Exchange Tadawul, beginning in 2018 after they partnered with Sustainable Stock Exchanges to boost ESG integration in the listed companies. Furthermore, they continued with this path in 2020 after announcing Saudi Companies being included in the MSCI index (SSE Initiative, 2018). These actions by the Saudi Stock Exchange are interesting because ESG awareness is usually promoted by governments and then integrated into Stock Exchanges, whereas here it seems the opposite occurred.

ESG is the approach used to evaluate the social and environmental sustainability of companies. Its three pillars–Environment, Social, and Governance–aim to promote responsible

and ethical practices among businesses. However, can be challenging to track ESG because there is not one main index used unanimously, as some indexes prefer specific criteria over others, which can cause confusion in tracking ESG in a business.

Social norms in different countries are another factor that influence ESG. Certain indexes may favor ESG metrics that are not common in certain countries, which can lower an ESG score for a business in something they cannot entirely control. For example, Deforestation in Environmental would be preferred by Brazilian ESG indexes due to the deforestation problems ongoing in Brazil, while ESG indexes in countries that do not have an ongoing deforestation issue would not weigh the issue as heavily. An ESG index that employs the same metrics for every country will likely provide inaccurate results, which is why it'll be important to use a variety of indexes to measure ESG rather than relying on one.

One of the main selling points for integrating ESG into a business is that a more sustainable future that can technically benefit companies in the long term, but is this always the case? This paper analyses various Saudi Arabian companies and measures their performance based on their ESG rating to determine if their rating can be a viable investment metric in the Saudi Stock Exchange (Tadawul). This will be done using historical return data and a standard portfolio evaluation model.

Literature Review

In 2021, Murad Ali conducted a notable study on ESG practices in Saudi Arabia, a relatively underexplored subject in this region. The study revealed a significant gap in ESG reporting among Saudi companies, with a limited number of them publishing Social Reports. This lack of comprehensive ESG data presents challenges for investors who are focused on ESG stocks, as it hinders their ability to effectively track and assess the performance of these stocks. The findings from this study suggest that the ESG market in Saudi Arabia may not yet be mature enough for effective implementation and investment, underscoring a need for enhanced ESG disclosure and reporting practices within the Saudi corporate sector.

Hussein Mohammad Salameh (2020) applied the 5-factor model on the Tadawul exchange and compared it to the CAPM and the 3-factor model. The author found that the 5-factor model does not necessarily have an advantage over the 3-factor model and CAPM. Additionally, they conclude that, due to the nature of the Tadawul exchange being different to the rest of the world due to Islamic Sharia, finding accurate results can be challenging due to complicating the return determinants.

The study conducted by Simin Chen in 2023 focused on investigating the impact of ESG on financial performance, specifically examining whether this relationship is moderated by digital transformation. The study utilized data from A-share listed companies in China, spanning from 2015 to 2021, to test this mechanism. The dataset comprised 15,710 unbalanced panel datapoints from 2,256 listed companies, excluding certain types of companies and those with missing data or high debt-to-asset ratios. ESG data were sourced from the Huazhong ESG rating

system and financial data from the China Stock Market and Accounting Research (CSMAR) database and the National Bureau of Statistics.

The study adopted return on assets (ROA) as the dependent variable to reflect resource allocation efficiency, and ESG performance was measured using the Huazhong ESG rating system, which assigns grades based on quarterly ESG ratings. These grades range from 1 to 9, with higher scores indicating better ESG performance. For measuring digital transformation, the study conducted text analysis and word frequency statistics on the annual reports of listed companies, focusing on elements like AI technology, Big Data, cloud computing, blockchain technology, and digital technology application. This analysis utilized Python and the "jieba" word segmentation tool. The regression analysis revealed that ESG performance significantly and positively affects corporate financial performance, as indicated by ROA. This positive effect persists even when accounting for lag periods, suggesting a consistent influence of ESG on financial improvement. The study found that the enhancement effect of ESG on financial performance varied, being significant for non-state-owned companies and those in the eastern region of China, and more pronounced for polluting firms compared to non-polluting ones. The 2023 study by William T. Smith analyzed the impact of ESG practices on stock returns in the US market from 2002 to 2020. The study replicated earlier research indicating that while socially responsible funds previously underperformed, this trend has diminished in recent years. The findings revealed that regardless of the ESG database used, neutral stock portfolios consistently showed higher systematic risk (beta) than ESG portfolios, although this gap has narrowed over time, likely due to increased demand for ESG portfolios. Contradicting earlier literature, the study found that risk-adjusted returns varied significantly based on the ESG rating provider and did not consistently support the underperformance or superiority of ESG portfolios over time. This inconsistency led to the conclusion that the "ESG label" alone is not a definitive factor in determining portfolio performance.

Eraslan (2013) used the three-factor model in the Istanbul Stock Exchange based on monthly data spanning seven years,and the paper concluded that the book-to-market ratio has a significant effect in the Istanbul Stock Exchange, more specifically the firms with a high book-to-market ratio. This is significant and will be one of the factors used in this study, and with Istanbul having similar Islamic Sharia laws as the Tadawul Exchange.

Shaker & Khairy (2014) used five different models on the Egyptian Stock Market to compare the data they have gathered, and the models included CAPM, Fame & French three-factor model, the Carhart four-factor model, Fame & French five-factor model, and the liquidity-based four-factor model. The study used six portfolios based on book-to-market ratio and size. The study concluded that the Fama & French three-factor model was the best option. Similar to Eraslan (2013), with the Egyptian Stock Market having similar Sharia Laws to Tadawul, the results found here can be interesting to compare to the result of this paper. Theoretical Passage

Efficient Market Hypothesis

The Efficient Market Hypothesis (EMH), posited by Fama and French in 1970, forms the foundational premise of this paper, which aims to discern whether ESG investing yields superior returns compared to non-ESG stocks, and more critically, if it is possible for an investor to consistently outperform the market through sustainable investing. EMH asserts that asset prices fully reflect all available information, suggesting that beating the market consistently on a risk-adjusted basis is unfeasible. Fama and French categorized market efficiency into three forms: weak-form, examining historical price information; semi-strong form, considering public information beyond historical prices; and strong-form, focusing on private information. Fama-French Three-factor and Carhart four-factor models

The Fama-French Three-Factor and Carhart Four-Factor Models are pivotal to this discussion. The Fama-French Model, introduced in 1992, aims to explain stock return fluctuations. It was a natural choice for regression analysis in this thesis, given its relevance in examining the performance differential between ESG and non-ESG companies. This model includes the market-to-book factor, reflecting a firm's earning potential relative to its book value, and size, linked to profitability. Fama and French's findings indicate that, controlling for book-to-market equity, smaller firms often have lower earnings on assets compared to larger firms, known as the size effect. This model also incorporates the market factor, acknowledging that size and book-to-market factors alone can not fully explain the variance between average stock returns and risk-free returns. The Carhart Four-Factor Model further enhances this analysis by including momentum as an additional factor, based on the observation that stock prices tend to continue their existing trends.

Jensen's Alpha

Jensen's Alpha, introduced by Fama and French, is a metric for gauging a strategy's ability to surpass market performance. It signifies a strategy's "edge" or "excess return" and is used to determine the abnormal return of a security or portfolio over its theoretically expected return. In this study, Jensen's Alpha measures the marginal return of investing in ESG companies against a standard market portfolio, like the Hang Seng Top 50. Alpha, the intercept in regression equations, can be positive, negative, or zero, reflecting the performance of an investment relative to a benchmark index.

Capital Asset Pricing Model

Finally, the Capital Asset Pricing Model (CAPM) is an essential component of this analysis. CAPM is a model that models the relationship between the expected return of an asset and its risk, quantified by its beta, which measures the asset's volatility relative to the market. CAPM posits that the expected return on an investment is a function of the risk-free rate of return, the investment's beta, and the market's expected return. This model provides a theoretical framework to assess whether the risk-adjusted returns of ESG investments differ significantly from those predicted by the market. In the context of this paper, CAPM serves as a benchmark to

evaluate the performance of ESG stocks against market expectations, offering insights into the viability and effectiveness of ESG investing as a strategy to achieve superior market returns.

Hypothesis

While ESG metrics offer valuable guidance for businesses to enhance their sustainability and practices, they also entail significant costs. Most ESG-focused changes lead to increased expenses for companies. For instance, adopting clean energy solutions necessitates substantial capital investment, yet profits may not immediately reflect this investment. This financial burden of adopting ESG practices is a likely reason for the slower adoption of ESG practices in Saudi Arabia compared to other regions, where there is less government and consumer pressure to implement such changes.

The growth of ESG in Saudi Arabia is further hindered by the absence of mandatory reporting requirements for companies. The lack of publicly available ESG data makes it challenging to ascertain whether a business is adhering to ESG principles. This situation arises from a lack of regulatory enforcement and minimal consumer demand for ESG compliance, offering little incentive for companies to disclose their ESG efforts.
Additionally, businesses focusing on ESG initiatives might need to redirect resources from their core functions. Significant investment in ESG infrastructure, including the hiring of specialists, can divert financial and human resources, potentially impacting profitability. This shift in focus and resource allocation may be viewed unfavorably by investors, especially if it leads to reduced financial performance.

The absence of standardized ESG metric reporting in Saudi Arabia complicates the ability for investors to compare and evaluate businesses, potentially deterring them from investing in ESG-focused companies. Furthermore, since ESG initiatives are typically long-term endeavors, they may not align with the short-term performance expectations of some investors. Businesses embracing ESG practices might face the need to increase their prices to cover the costs of sustainable operations. While a segment of consumers may appreciate and support these sustainable efforts, a significant portion might react negatively to higher prices, potentially forming an adverse opinion of ESG initiatives. However, for those consumers who value sustainability, this could enhance brand loyalty and return business, highlighting that despite the challenges, effectively implemented ESG practices can contribute positively to a company's profitability and public image.
H0: ESG stocks cannot outperform regular stocks on a risk-adjusted basis.
H1: ESG stocks can outperform regular stocks on a risk-adjusted basis

Methodology

This paper utilizes the Carhart four-factor model for analysis, which is a modified version of the Fama & French three-factor model. The initial three-factor model uses Market Risk Factor, Small Minus Big (SMB), and High Minus Low (HML). Respectively, these assess the excess return of the market; the historical outperformance of small stocks over big stocks; and

the difference between value and growth stocks, with the assumption that value stocks outperform growth stocks. In Carhart's model, a fourth factor is added Momentum (WML). Momentum accounts for the historical run of a stock and argues that historically well-performing stocks will continue to perform well. Using the Carhart four-factor model will provide a regression to be able to analyze the results and answer the question this paper aims to find.

Data

Given the recent introduction of ESG rankings in Saudi Arabia and that the rankings have recently been established, I compiled the companies used in this paper from ESG Invest (Sustainability Excellence, 2023), taking the highest 50 ESG-ranked companies in the Tadawul Exchange. ESG Invest creates its ranking based on "ESG data points across 9 Sustainability Dimensions and 43 ESG issues with more than 180 data points for companies in the Arab world". A lack of ESG rankings in Saudi Arabia severely limited which one I could pick, and ESG Invest seemed like the best option in this regard. The companies were separated into five quintiles, from the ten best to the ten worst ESG rankings, with Portfolio 1 being the ten best. Yahoo Finance was used to capture the 50 chosen companies' monthly share prices from January 1, 2018 - August 1, 2023. The monthly return was calculated by ((New Month Price - Old Month Price) / Old Month Price). The Carhart four-factor model data was taken from Kenneth R. French - Data Library, using the developed market factors, as to a lack of data available in Saudi Arabia and the Middle East. The market factors included Small Minus Big (SMB), High Minus Low (HML), Risk-free rate (RF), Market Risk-free rate (Mkt-RF), and Momentum (HML).

Empirical Results

Table 1 - Portfolio Regression Analysis

		Alpha	Mkt-RF	SMB	HML	Momentum	Observations	Adjusted R-squared
Portfolio 1	beta	0.007474	-0.00173	0.004312	-0.00195	-0.001051	68	-0.013758502
	p-value	0.010709	0.240756	0.281785	0.327869	0.6707391	68	
Portfolio 2	beta	0.015368	-0.00164	0.003117	-0.00303	-0.001551	68	-0.013615801
	p-value	0.038315	0.305198	0.474029	0.164504	0.5649872	68	
Portfolio 3	beta	0.011217	-0.00207	0.00478	-0.00256	-0.001056	68	-0.016075077
	p-value	0.185261	0.26229	0.341642	0.307719	0.7339602	68	
Portfolio 4	beta	0.009759	-0.00069	0.009168	-0.00408	-0.001278	68	0.020942641
	p-value	0.301641	0.736588	0.105496	0.147741	0.7131027	68	
Portfollio 5	beta	0.009726	-0.00048	0.009622	-0.00421	-8.52E-05	68	0.006860017
	p-value	0.387628	0.844465	0.153528	0.209833	0.9835899	68	
Portfolio 6	beta	0.010709	-0.00132	0.0062	-0.00316	-0.001004	68	0.000805078
	p-value	0.181978	0.448716	0.194452	0.183964	0.7328983	68	

Note: Carhart Four Factor Model data from Dartmouth Kenneth R. French - Data Library (January 1st 2018 - August 1st 2023). Monthly share prices from Yahoo Finance (January 1st 2018 - August 1st 2023)

In the regression analysis for the portfolios, key statistical metrics such as alpha, p-value, and adjusted R-squared are included. These metrics play a crucial role in hypothesis testing, particularly in determining whether to reject the null hypothesis. The null hypothesis, in this context, posits that ESG stocks do not outperform regular stocks.

The criteria for rejecting the null hypothesis primarily hinge on the p-value, a measure of the probability that the observed results would occur under the null hypothesis. Typically, a p-value threshold (often set at 0.05) is used; if the p-value is less than this threshold, it suggests that the observed results are statistically significant, and the null hypothesis can be rejected. In this analysis, Portfolios 1 & 2 have p-values below the threshold, leading to the rejection of the null hypothesis. This supports the idea that ESG stocks outperform regular stocks in these portfolios.

Conversely, Portfolios 3-5 and Portfolio 6 have p-values above the threshold, indicating that the results are not statistically significant enough to reject the null hypothesis. Therefore, for these portfolios, there is not sufficient evidence to conclude that ESG stocks outperform regular stocks. In fact, for Portfolio 6, which comprises all 50 ranked companies, the inability to reject

the null hypothesis suggests that investing in a broad portfolio of ESG stocks might not yield better returns than regular stocks and could sometimes be less advantageous.

The measure of uncertainty, indicated by the high p-values in Portfolios 3-5, also casts doubt on the reliability of the alpha values. Alpha represents the excess return of a portfolio over its expected performance, based on its risk profile. However, when the p-value is high, it implies a greater degree of uncertainty about whether the observed alpha is due to genuine outperformance or merely random chance. In such cases, high p-values reduce the credibility of the alpha values, suggesting that the apparent outperformance might not be reliably attributed to the portfolio's characteristics but could be a result of random fluctuations or other unaccounted-for factors.

Limitations & Extensions

The exploration of whether ESG companies in Saudi Arabia outperform market risk factors, as evidenced by the empirical study from the Tadawul, reveals significant limitations that impacted the study's outcomes. A pivotal constraint was the use of monthly prices rather than daily, which led to a smaller sample size. This limitation is crucial as it potentially undermines the reliability of the data, given that a larger data set could provide more robust and statistically significant results. Smaller sample sizes often result in less reliable data due to increased susceptibility to outliers and reduced power in detecting true effects.

Another significant limitation was the restricted scope of companies included in the study, constrained by the lack of comprehensive ESG data in the Saudi Arabian context. Expanding the range of companies analyzed could have potentially offered a more representative picture of the ESG landscape in Saudi Arabia. However, the lack of available ESG data limited this possibility, potentially biasing the results.

The low Adjusted R Squared values observed across all portfolios suggest that the market risk factors might not be a suitable fit for this particular analysis. This finding indicates that these factors may not accurately track or predict future market expectations within the context of ESG investing in Saudi Arabia. This aspect raises questions about the appropriateness of the market risk models used and suggests a need for models that better capture the nuances of ESG investing in the region.

A notable observation was the significant difference between Portfolios 1 & 2 compared to 3-5. This discrepancy could indicate a unique characteristic inherent in the first two portfolios. Intriguingly, Portfolio 2 exhibited twice the alpha of Portfolio 1, implying the portfolio has performed better than would be expected given its risk level. This difference could stem from factors not captured in the model or discrepancies in the accuracy of the ESG ranking. The composition of Portfolio 2, predominantly banks and telecommunications companies, may have contributed to its superior performance, reflecting the sectors' growth in line with recent increases in economic spending and activity in Saudi Arabia. This sector-specific performance could indicate that certain industries may be better positioned to leverage ESG principles for enhanced market performance.

Conversely, Portfolio 5, which had the highest p-value, included three cement companies. The presence of these companies might have negatively influenced the portfolio's performance, considering the typically lower sustainability metrics associated with the cement industry. This finding suggests that industry-specific factors play a critical role in determining the efficacy of ESG investing and its impact on market performance.

Overall, these insights highlight the need for a more refined approach to analyzing ESG performance in Saudi Arabia, one that accounts for the specificities of the Saudi market and the limitations posed by available data. Future research could benefit from incorporating a larger sample size, more frequent data points, and a broader range of companies to provide a more comprehensive understanding of the relationship between ESG practices and market performance in the region.

Conclusion

In conclusion, this paper investigated whether ESG companies in Saudi Arabia outperform non-ESG companies, revealing mixed results. While Portfolios 1 & 2, predominantly consisting of banks and telecom companies, exhibited a significant outperformance of regular stocks, this was not observed across all portfolios. Limitations such as the use of monthly data and a lack of comprehensive ESG data affected the reliability of the findings. The study underscores the importance of industry-specific factors in ESG performance and highlights the need for more detailed ESG reporting and analysis tailored to the Saudi market. Future research should focus on expanding data sources and incorporating a broader range of companies to assess the impact of ESG practices more accurately on market performance in Saudi Arabia. To deepen the understanding of ESG's influence on market performance in Saudi Arabia, future research should adopt a multifaceted approach. Expanding the data collection to include daily pricing and a diverse array of companies, including smaller enterprises, would offer a richer dataset for analysis. Longitudinal studies could reveal evolving ESG trends over time, providing insights into long-term impacts. Sector-specific analyses are crucial, considering the varied ESG effectiveness across industries. Comparative studies with similar economies or regulatory environments would contextualize Saudi Arabia's ESG performance globally. Additionally, assessing the influence of regulatory changes on ESG integration and examining consumer and investor behaviors towards ESG could offer valuable insights into market dynamics and preferences.

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Stock Investment's Telescopic Visibility into the Economy By Yohan Hong

People obtain a broader perspective on macroeconomics and innovations by investing in stocks. Macroeconomic and technological analyses of the innovations that occur in the banking, automobile, and semiconductor sectors present themselves as examples of opportunities stock investment provides to gain more insightful key insights into macroeconomics and innovative industries. Detailed technical examinations of the rising innovative functions that can unlock incomprehensible growth potential convey the powerful and upgraded features that distinguish them from past developments. For example, the majority of the people of the 21st century acknowledge the inseparable necessity of semiconductors in their daily lives. But, many are not informed of the structure and functions of semiconductors, which gives an answer to the why and how the little chips are innovations. Besides the technical refinements in innovative developments, the historical background behind the technological innovation comes prior to the look at the future or current technological improvements because it spotlights the needs in the past and present that sparked ideas for innovation. However, the ultimate role of macroeconomic situations and the Federal Reserve System's policies in determining the path of the financial/banking sector invalidates the need for an investigation of technological innovation in the industry. Instead of observing technological advancements, a thorough look at the revolutionary changes in the Fed's recent stance towards the economy and the stock market allows one to view and learn the macroeconomic lessons the financial industry holds.

The undetachable connection between the Fed's monetary policies and economic circumstances and the performance of the banking sector leads people to inevitably be aware of the macroeconomic conditions. The financial industry is a sector most sensitive to economic swings and the decisions of the Federal Reserve System, the central banking institution of the United States of America. People's willingness to borrow money from the banks and healthy credit status create favorable conditions for banks. The fundamental profit source of banks is the gain produced from the difference between long-term bond rates and short-term bond rates, also known as deposit margin. Since the Fed's monetary policies direct the whereabouts of bond rates and interest rates, tracking the movements of the Fed is vital. Alongside the Fed, economic conditions are an original game-changer of the financial industry.

An economic phase where people are not hesitant to lend and make loans can lead to an ideal type of inflation: inflation triggered by an increase in wages. When people work with more wages, they are willing to open their wallets and purchase goods. In other words, consumption is prominent. More spending leads to a profit increase for companies and attracts them to expand production lines/capacities of their products to accommodate the rising demand. In the process of expanding production lines, companies also increase employment. In addition to opening work opportunities for more people, companies make loans from banks to make investments for additional production lines. The illustrated scenario is a representative case of what people refer to as a "good economy," because such a type of economy mirrors the active presence of consumption and credit. An economy with a high currency multiplier and consumption allows

the price of nominal treasury bonds to fall and the yield attached to the bond to rise. The segment of wage inflation in which companies make loans from banks to make investments foster profitable conditions for banks.

The Fed recently signaled an implementation of quantitative tightening after the 7.6 trillion dollars quantitative easing, which had taken place over the course of the past two years since the outbreak of the coronavirus pandemic. Quantitative tightening is the opposite process of quantitative easing. The procedure indicates that the Fed will execute both tapering, a slowdown in the speed of asset purchases, and a rake hike – a raise in interest rate differs from a rise in interest rates in that the Fed passively changes it. Quantitative tightening is an example of an auspicious impact of the Fed on the banking industry because as the Fed sells the long-term treasury bond they purchased, the long-term treasury yield rises, and the deposit margin increases concurrently.

Covid-19 foretold no signal for its unexpected appearance and is continuing to linger on our planet, taking the lives of thousands. Along with all the tragedies the virus brought, lockdowns have been lethal and poisonous enough to create hundreds of billion dollars worth of revenue losses in the semiconductor and automobile sector. The ungraspable spread of the virus rendered it inevitable for Southeast Asian countries, like Malaysia and Singapore, to get into lockdowns. Shutdowns in factories in Southeast Asian countries are deathly because they are major suppliers of semiconductors. Take STMicroelectronics, a French-Italian semiconductor producer, for example. Technology reporters for Bloomberg L.P. Yoolim Lee and Yantoultra Ngui publicized that the semiconductor company was not able to supply chips to world-leading customers of semiconductors such as Apple Inc. and Tesla Inc. Cars are big consumers of semiconductors – each car can require up to 3,000 chips (Lee & Ngui).

Average inflation targeting is an unprecedented path the Fed took to convey its supportive stance of the stock market 2020. Prior to touching upon the original policy, a supplementary recap to the history of how the Fed transformed from an inflation fighter to a deflation fighter is critical. As President Richard Nixon terminated the gold standard in 1971, a policy in which an ounce of gold was fixed to a price of 35 dollars, it was nowhere to be seen from the world, and the United States began to print dollars as much as the core inflation was not excessively bothered by the circulation of the currency; the U.S.A. could release as much as liquidity they desired to. Naturally, inflation soared with the swift injunction of cash. The fearful inflation had aggravated as the Organization of the Petroleum Exporting Countries drastically tightened oil production. Oil prices skyrocketed and fueled dreary inflation. From that point on, the Fed had developed a firm identity of the world-leading inflation fighter. The formulation of the new identity was characterized by the former Fed Chairman Paul Volcker's bold rate hike. Bolker countered it by raising the federal fund rate, the interest rate applied when U.S. banks make transactions within one another, to 20% in 1981. But, according to Kun Young Oh, the Deputy General Manager of Shinhan Bank Co., Ltd., deflation and its subsequent consequences transformed the Fed to progressively transition away from inflation and switch its main opponent to deflation (Oh). The Japanese real estate bubble, a traumatizing and indelible event that created

devastating stagflation, the global financial crisis of 2008 led the Fed to prioritize counter-deflation policies over those for inflation. On top of an incomprehensible sized quantitative easing, the Fed adopted a policy named average inflation targeting in 2020. Average inflation targeting signifies the Fed will not retrieve liquidity until the average inflation rates of the recent four years meet the eye line of the Fed's standard 2% inflation rate. Throughout the past few years, specifically referring to years 2017 through 2019. inflation rates of the United States came short of the standard 2% rate by 0.5%. These policies have successfully convinced the stock market that the Fed will always stay on the right side and support it with liquidity. The stock market experienced a minor correction intermittently, which ranged from a 3 to 5% drop since March of 2020 but it has not encountered a major one until last November.

The key to producing successful returns in the financial industry is a close observation of the direction of inflation. As long as inflation remains present, the banking stocks are likely to outperform the performance of the market. They may undergo some forms of turbulence or fluctuation when tech stocks rebound and the Fed's view towards inflation changes frequently. Jeanna Smialek, an economy reporter for the American daily newspaper New York Times, demonstrates that Jerome Powell, the head of the Fed, did not provide straightforward guidance on the Fed's future policies as he stressed the importance of the Fed in remaining "humble and nimble" (Smialek). Many different interpretations have been proposed, but one can approach Powell's comments by focusing on the Fed's capricious comments on rate hikes. The underpinning intention behind the Fed's inconsistency may come from the Fed's effort to alert people with precedence and observe the market's reaction before determining the number of rate hikes. As the stark taper tantrum in 2014 reprimanded the Fed, the Fed's "goal is never to surprise people", remarked Claudia Sahm, the director of macroeconomic research for the Jain Family Institute and a former Fed economist (Sahm).

The current market only raises the hands of companies with robust earnings and reacts flatly to companies with disappointing earnings or/and untransparent earnings guidance. The Meta Platforms, Inc., widely recognized as Facebook Inc., represented the dire consequence for companies with short-of-expectation earnings in the current market atmosphere as its equities plunged 26.39% on February 3rd, 2022. The financial industry stands on the opposite pole. Having strong earnings as the base, banks like Wells Fargo & Company and Bank of America each rose about 15% from the six-month interval of August 19, 2021, to February 18, 2022, whereas the S&P 500 Index went down one percent during the same time interval. As numerous experts predict, the current inflation will remain durable until factories resume their operation and the global supply chain shortage gets mitigated or tackled. The Fed will also continue to implement liquidity-tightening policies as long as the economic conditions are healthy. Last December, U.S. employment showed a drastic increase as the unemployment rate dropped down to 3.9%, a symbolic number that signifies the employment market is now as healthy as it used to be prior to the outbreak of coronavirus. Economy reporters for the Bloomberg L.P Olivia Rockeman and Read Pickert inform that Powell trusts the current employment rate is robust enough for the economy to accommodate tapering, raise in interest rates, or other forms of

policies that retrieve liquidity, "Most FOMC participants agree that labor market conditions are consistent with maximum employment in the sense of the highest level of employment that is consistent with price stability" (Rockeman and Pickert). Rebound in employment is critical in leading the Fed to avert its main attention to price stability because it reflects the economy is robust enough to encounter policies for tackling inflation, which has the potential to pose a threat to the current vigorous economy. The performance of the financial industry will trace the footsteps of inflation and the spread between the 2-year treasury bond yield and 10-year treasury bond yield. The bigger the gap between the two, the better for the financial industry as the enlarging margin increases the Net Interest Margin(NIM). As mentioned previously, the profit of the banks comes from the difference between the interest rate banks receive for providing loans and the deposit interest rate the banks yield to the public. However, when the Fed's attitude and economic indicators signal a weakening in inflation, the financial stocks will lose their momentum as investors transport their funds to tech-growth companies. Historically, two black-and-white scenarios have existed in the stock market: either equities of inflation-favoring sectors, such as food and beverage; energy; and banking are the only ones on a roll or fast-growing technology equities rise and nothing else. The current market atmosphere is the former case where consumer cyclical and the banking stocks are enjoying their showtime and growth technology equities are not. But, since the financial industry will not be welcomed as warmly as they are now once the inflation subsides, investors must diligently track the path of the current inflation. The Fed's actions to cope with undesirable economic circumstances become unavoidable areas to study in the domain of stock investment.

Variations in economic phases and abrupt shifts to establish a mobility-centered transportation system contribute to swings in vehicle sales, which demands people to examine the macroeconomic issues and technological step-ups in the automobile industry. Automobiles are an undetachable mode of transportation for any person of the 21st century. A detailed breakdown of the history of automobiles is unnecessary. However, taking note of the solid share of internal combustion cars in the automobile sector can lead one to appreciate the brisk advancements toward the new wave of innovation called the mobility ecosystem. The automobile industry is a cyclical business, meaning that economic conditions set the sentiment of automobile purchasers. People decide to purchase automobiles when their financial status is adequate enough that it provides confidence or room to reach out for consumer discretionary products. Consumer discretionaries pertain to peripheral products people seek to buy when they possess sustainable income. The value of a vast majority of consumer discretionaries sways according to variations of consumer preferences and qualities of products. Since income status links with swinging demands for cars, employment and changes in interest rates are critical to automotive players. Low-interest rates and high employment rates allow people to increase spending whereas high-interest rates and poor employment cut spending. Stable income gives a sense of trust and clarity in one's financial status.

Automotive players of a couple of years ago were manufacturing companies. They had been following the equation of the more cars produced, the more profit they gained–mass

manufacturing is the overarching theme of the automobile producers. But, the current, long-held business structure centered in mass manufacturing of gasoline and diesel cars has two limitations for survival: the rapid alternation in customer trends and global advancement to cope with climate change. The young generation's preference in transportation directs to vehicle sharing service usages' overtake of the idea of personal car ownership. Leanna Garfield, a former reporter for Business Insider Inc., whose works were presented in the World Economic Forums, assesses that no consumer of the U.S.A. will own personal cars in 2030 (Garfield). In addition, data from the American news channel CNBC mirror the continuous decline in car shares and the already-changing trend of car consumers. Olivia Raimonde, a former reporter for CNBC, delivers that the number of global passenger car sales in 2018 recorded 80.6 million, a number coming short of that of 1.2 million recorded in 2017 (Raimonde). The international trade association Organization Internationale des Constructeurs d'Automobiles also reports the annual decline in global car sales continued through 2020, as only 63,730,387 and 53,598,846 passenger cars were consumed during the year 2019 and 2020 respectively ("Sales Statistics"). The linear style of decline in demand for passenger cars potently demands automotive manufacturers to recognize the rapid shift in consumer trends and adopt new qualities and approaches that are aligned with consumer demands.

The alternated consumer preference towards the transportation system reflects the emergence of mobility ecosystems, and in the core of the new phase of automobiles lies autonomous driving and 5G technology. Integration of the two features into the automobile sector creates synergies beyond efficiency. One key benefit is the unity of devices. Cars of these days are not capable of exchanging signals or codes–each device is on its own. However, interconnected devices and the formation of a communication web open space for autonomous driving and 5G technologies to shine. Advanced driver-assistance systems(ADAS) is one of many autonomous driving technologies that follows the development of communicating cars. Autonomous driving technology is divided into six stages of completion, and ADAS belongs to the second level. Vipin Kukkala, a Ph.D. student in the Electrical and Computer Engineering Department at Colorado State University, and others reveal that ADAS technology enhances drivers' safety by alerting surrounding objects to the driver and maintaining safe distance and speed of the car (Vipin et al.). Taking a step further, the harmony between Vehicle to Everything(V2X) technology and ADAS advances driver's safety and efficiency by another level. V2X technology communicates with vehicles, infrastructure, like bridges, roads, and pedestrians through 5G requiring equipment. The method of communication shares similarities of how people communicate through phones and tablets.

The global movement to generalize green-field vehicles in response to daily-aggravating climate change is another impediment to traditional OEMs. OEMs that possess their own electric vehicle(EV) platform and actively create joint ventures with other companies will thrive, but OEMs that do not take a flexible approach to the fast-changing industry will not survive. As Ankit Jain, a former Director of Engineering at Google LLC and the founder and Chief Executive Officer of Infinitus Systems, Inc., unveils, governments across the planet are placing

regulations and making fearless investments to minimize carbon emission from automobiles (Jain). A bold example is presented by the McKinsey Company which informs the Italian government has played a crucial figure in leading bike shops to run out of stocks by providing subsidies/bonuses worth 500 euros. In addition, the Massachusetts Institute of Technology demonstrates that China has required Chinese automakers to raise the percentage of EVs in proportion to their total production to 40t% by 2030. Since regulations to make OEMs transition to EV have been and will stay omnipresent, OEMs must make daring investments to expand productions for green energy vehicles and to remain coherent with new customer trends.

Both the state of investment morale and profitability will move in line with those of the semiconductor sector. The causations of the continuing correction in the automobile sector are inflation and semiconductor supply chain disruptions; the semiconductor and automobile industry are grappled down by identical forces. While the market does not regard the automobile stocks as tech stocks as it does to semiconductor equities, semiconductor shortage is the primary obstacle for the automobile industry. The recent tumble of the equities of Tesla, Inc. corroborates the strength of the broken semiconductor supply chain. Throughout last November and December, the world-dominating electric automobile producer has again boasted its fast-growing production rate and cheered the investors by hinting them of two million vehicle sales for 2022. During the one-month interval, the company's stock soared up to the 52 week-high of 1,243.49 dollars for a share and hit one billion market capital. The air of blooming spring faded away as concerns for the decline in car sales led by forecasts of persisting semiconductor shortages. The opening gate for investment in the automobile industry is the same as that of the semiconductor sector: recovery of the on-time semiconductor supply and demand cycle.

However, investors need to take prudent considerations prior to opening investment positions in the automobile sector. When an industry enters into a new stage of development that overturns the old structure, new players also step into the game field and pursue a shared goal to acquire market share with heated competition. Unfortunately, competitive nature dampens investment sentiment because the ambition to achieve an identical object inevitably lowers the chance for all companies to take a solid proportion of the industry. As discussed above, oil-fueled automobiles no longer sit on the throne of the automobile industry–green energy vehicles do. Automobiles powered by self-driving technology and green energy are the heart of the automobile industry, and the transition has already occurred less than five years ago–the automobile sector is in a novel portion of development. In a new phase of an industry, companies that possess superexcellence – technologies that grant a limited number of companies ascendancy from the new-born, emerging players–initially become the leaders and occupy a good amount of the industry's market share. While nothing can affirm the initial leader will continue to be the leader in the future, since the data and production capacities that have been accumulated throughout the span of multiple decades hands the pioneering companies their preceding status, they will hardly concede their dominance to other companies. The return of the automobile industry exhibits an anchored association between the cyclical nature and rapid

replacement of the conventional business structure of the sector.

The global expectation for flawless, uninterrupted supply of semiconductors and continuous investments to meet demands for more compact and faster processing chips require people to trail along the economic circumstances and the semiconductor sector's progression to refined stages of technology. Throughout history, the semiconductor sector has experienced a series of upswings and downswings within intervals of two years or shorter. A customary cycle of the price of semiconductors commences as demand for semiconductor chips becomes solid. The popularity of the chips gives the chip producers a higher level of profit, which is reflected by the robust return of their publicized stock shares. Then, the surging popularity entices the chip producers to expand their production line to accommodate the demand. The activating force for the strong upbound for chip usages normally takes a shape in the emergence of innovative services that ask for greater quantities and more compact chips. However, as nothing can last perpetually, the extension of production lines condones the supply to override the demand. Semiconductor consumers, in this case referring to companies with their products or services powered by semiconductors, do not feel the necessity in sweeping the chips in urgency – consumers form a consensus to gather semiconductors with all their will when they believe the competition to possess the chips becomes evident. Their interest in stockpiling the chips from the producers revives when the quantity of the chips in the inventory shrinks and acknowledges the urge in purchasing the chips before other competing companies take possession of them. Such a phenomenon is salient and a distinct characteristic of cyclical industries. However, the high correlation between the supply and demand cycle and the profitability of the semiconductor players places the semiconductor industry in an antiparallel position to other traditional cyclical sectors. Unlike the traditional cyclical industries like steel or chemical fields, macroeconomic factors are less impactful to the semiconductor sector. The macroeconomic factors are still influential, as the following examination will confirm, but the supply and demand cycle within the semiconductor industry is the genuine game-changer.

Since Intel Corporation released their CPU manufactured in the 14-nanometer manufacturing process with its fin field-effect transistor(FinFET) in 2012, the company has not shown a system semiconductor that requires a more advanced DRAM to go along, which has laid a huge obstacle in improvements of speed in DRAM. But, how does Intel's stationary stance towards the development of their CPUs or systems semiconductors connect to a long delay of upgrades in the speed of DRAM? Intel is undeniably the largest and most influential supplier of system semiconductors, especially CPUs of personal computers and corporate servers. Intel's processors have permeated deep enough that people likely use them almost daily; they are omnipresent. Intel's customers include Microsoft Corporation; Amazon.com, Inc.; and Dell. However, nearly a decade of time has passed since Intel launched their CPU processed under a 14-nanometer manufacturing technology. 10 years was sufficient time to nullify Moore's law, which states the number of transistors in integrated circuits doubles every two years. Engineers and researchers appraise Intel's new project "Sapphire Rapids" to mark the end of the dark tunnel. Sapphire Rapids represents Intel's new processor manufactured in a 10-nanometer

SuperFin process based on the Embedded Multi-Die Interconnect Bridge technique. The processor integrates four silicon chips that embrace internal circuits and form a shape of a monolithic chip. Companies have loved the monolithic design in the past because of its simplicity and fast data transmission speed, but as demands for small-sized chips with smaller nodes override the past trend, the production yield of monolithic design chips has decreased simultaneously. The alternative to the monolithic structure is the microservice design, which separates dies into independent units. However, as demonstrated by Dr. Ian Cutress, the Senior Writer for Anandtech.com, the structure of Sapphire Rapids proved that Intel did not follow the long-held preference (Cutress). Through Sapphire Rapids, Intel took advantage of both the strengths of the monolithic and microservice applications. An assembly of dies on an interposer opens more space to spread information and reduce the chances of latency caused by leakage current. The memorable advancement in the structure of Intel's processors will stimulate the current DRAMs to step up and become equipped with faster data transportation speed, opening a new stage for DDR5s. A DDR5 ram will deliver data with the maximum speed of 7.2 billion bits per second(Gbps), a number nearly as two times that of a DDR4 with a maximum rate of 3.2 billion bits per second. Prospects of a DDR5 ram are bright as experts expect supercomputers, enterprise servers, and data centers to act as pioneers for drawing demand for the cutting-edge rams.

The current gravitational pull of the semiconductor sector is the disruption in the supply chain enforced by shutdowns in factories of semiconductor producers across the world. The White House evaluates the unanticipated eruption in demand for personal electric products as fundamental causation of the chip shortage, and the impact of the issue has spread to suppression of automobile sales and communication service productions (The White House). While the cut in the global semiconductor supply chain has coerced the semiconductor sector to involuntarily enter into a lingering correction phase, the fundamental value of the industry has not been harmed. Inflation and rate hikes can debilitate investment sentiment as the stock market categorizes the semiconductor sector into a tech industry. Sectors with technological development as their main profit source are vulnerable and do not make desired returns during inflation because the rising bond rates can damage their profitability. Investors praise the future profitability of technology stocks, which they forecast to be greater than the current profit, and they yield them high multiple values or price-to-earnings ratio(PER). But, rising interest rates depreciate the estimated future profit value. However, even cautious perspectives toward the semiconductor sector during inflation and rising interest rates cannot penetrate into the fundamentals of the industry and efface its title of the frontline industry of the 4th industrial revolution. Economic circumstances and monetary policies do not stop companies from expanding production lines. The essence of the minuscule chips smaller than human blood cells has been spotlighted more brightly than ever as the progress in the 4th industrial revolution has taken place earnestly and demands for green energy automobiles cars have surged. The global world is seeking out semiconductors with its neck out. The demand and supply cycle and continuation in global technological development may alternate the quality the semiconductor

industry holds. Therefore, the ongoing correction is an opportunity for investors to reevaluate the undervalued fundamentals of the semiconductor sector and slowly open positions. For investors who pursue a stable avenue, exchange-traded funds(ETF) that mirror the performance of the PHLX Philadelphia Semiconductor Sector index are recommended. The state of investment sentiment for the semiconductor sector and tech stocks are linked to the movements of the long-term bond yields–short-term bonds are bonds that expire in less than three years, and they cannot accurately reflect the future profitability of semiconductor players. Unless the cut in the supply chain gets repaired by reactivations of semiconductor production factories and the sky-rocketing 10-year treasury bond yield becomes settled, the semiconductor sector will continue to decline. But, once the supply chain issue begins to submerge or/and completely hides its presence, the semiconductor sector will likely exert a strong rebound and outperform the market since the industry's inner fundamentals are not dented. A scrupulous observation of the macroeconomic circumstances and technological evolution within the semiconductor industry enables one to obtain a complete understanding of the supply and demand chain, the power source of the welfare of the semiconductor industry.

A variety of different perceptions of the word stock investment exist. While some groups of people react with dismay and claim that stock investment is the fastest way that leads one's life down to the chamber of "failure," others believe stock investment is the best means of financial investment because stocks transcend the return of interest rates in banks, which cannot keep up with inflation rates. Swing trade or scalping can carry volatility, and certain aspects of the investment method may assume gambling as people pursue high returns in a short term. On the other hand, the practice of yielding stable returns over a long phase of time requires a series of self-development. Though the realm of stock investment asks for in-depth study and self-reflection, systemic practices of the demanded qualities nurture people by expanding their views on macroeconomics and emerging innovations. Macroeconomics and innovations offer people a wide facet of the economy as a whole because they lie at the core of the driving forces of the economy.

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Association Between Sexual Identity and Risk for Unintentional Injury and Violence among Youth By Caleb Choi

Abstract

The Youth Risk Behavior Survey data includes questions regarding unintentional injury and violence: Differences by sexual identity were analyzed for unintentional injury and violence among youth. No statistically significant differences in driving when drinking alcohol among all youth. Bisexual youth reported highest percentage that they were in a physical fight at school. No differences reported by sexual identity. Bisexual youth reported highest percentage of electronic bullying. All sexual minority groups were statistically more likely to have been electronically bullied compared to heterosexual youth. Other/questioning youth were statistically more likely to have been threatened or injured with a weapon on school property compared to heterosexual youth.

All sexual minority groups (21%-26%) were statistically more likely to have been bullied on school property compared to heterosexual youth 12%. All sexual minority groups (13%-14%) were statistically more likely to not go to school because they felt unsafe at school or traveling to or from school compared to heterosexual youth 6.6%. All sexual minority groups (16%-23%) were statistically more likely to have been physically forced to have sexual intercourse compared to heterosexual youth (5%).

This study purpose was to look for statistically significant differences by sexual identity for unintentional injury and violence. Unintentional injury and violence are an important public health topic for youth. Schools can play a vital role in reducing violence and unintentional injuries to youth by providing services and referral services to at risk youth.

Introduction

Unintentional injury and violence among youth is an important public health topic. This research aims to examine if there are any statistically significant differences by sexual identity in unintentional injury and violence related behaviors in youth. Behaviors that contribute to unintentional injury include: not wearing a seat belt, riding with someone who's been drinking. Behaviors that contribute to violence include physical fighting, bullying, were threatened or injured with a weapon on school property, did not go to school because they felt unsafe at school or on their way to or from school; and were ever physically forced to have sexual intercourse. Injuries and violence among youth have a substantial emotional, physical, and economic cost to society. According to the WHO, injuries and violence place a massive burden on national economies, costing countries billions of US dollars each year in health care, lost productivity and law enforcement. (WHO) Understanding the epidemiology of this public health problem can guide prevention efforts, help identify and reduce risk factors, and promote protective factors." (Ballesteros, M; Williams, D.; Mack, K.; Simon, T.; et al.)

The hypothesis is sexual minority youth have higher risk of injury and violence compared to heterosexual youth.

The Youth Risk Behavior Survey data includes questions regarding unintentional injury and violence: Bullying, threats, physically forced to have sexual intercourse, and avoiding school due to not feeling safe at school or traveling to or from school.

Results

Table 1. Seat belt use by sexual identity: Did not always wear a seat belt (when riding in a car driven by someone else)

Sexual Identity Year	Total	Heterosexual (straight)	Gay or lesbian	Bisexual	Gay, lesbian, or bisexual	Other/Questioning
2021	39.9 (35.3–44.6) 12,777	39.1 (34.5–43.9) 9,197	37.7 (31.2–44.5) 379	42.5 (38.1–47.1) 1,359	41.5 (37.1–46.0) 1,738	35.3 (31.0–40.0) 1,086

No statistically significant differences in seat belt use among all youth. Nearly 40% of all youth reported not always wearing a seat belt when riding in a car driven by someone else.
Table 2. Drinking and driving: drove when they had been drinking alcohol (in a car or other vehicle, one or more times during the 30 days before the survey, among students who had driven a car or other vehicle during the 30 days before the survey)

Sexual Identity Year	Total	Heterosexual (straight)	Gay or lesbian	Bisexual	Gay, lesbian, or bisexual	Other/Questioning
2021	4.6 (4.0–5.4) 8,673[†]	4.4 (3.7–5.3) 6,671	6.3 (3.1–12.5) 222	4.1 (2.5–6.4) 762	4.6 (3.0–6.8) 984	4.3 (2.3–8.1) 539

No statistically significant differences in driving when drinking alcohol among all youth.

Table 3. Were in a physical fight on school property (one or more times during the 12 months before the survey)

Sexual Identity Year	Total	Heterosexual (straight)	Gay or lesbian	Bisexual	Gay, lesbian, or bisexual	Other/Questioning
2021	5.8 (4.4–7.5) 16,418	5.1 (4.4–5.8) 11,867	3.6 (1.6–7.9) 504	5.4 (4.4–6.7) 1,752	5.0 (3.9–6.3) 2,256	4.5 (3.0–6.7) 1,400

Bisexual youth reported highest percentage were in a physical fight at school. No statistical significant differences by sexual identity.

Table 4. Youth were electronically bullied by sexual identity

Sexual Identity Year	Total	Heterosexual (straight)	Gay or lesbian	Bisexual	Gay, lesbian, or bisexual	Other/Questioning
2021	15.9 (15.0–16.8) 17,032	12.7 (11.8–13.6) 12,307	24.8 (19.8–30.5) 513	28.4 (25.1–31.9) 1,825	27.6 (24.4–31.1) 2,338	24.8 (21.7–28.1) 1,462

All sexual minority groups were statistically more likely to have been electronically bullied compared to heterosexual youth.

Table 5. Were threatened or injured with a weapon on school property (such as a gun, knife, or club, one or more times during the 12 months before the survey)

Sexual Identity Year	Total	Heterosexual (straight)	Gay or lesbian	Bisexual	Gay, lesbian, or bisexual	Other/Questioning
2021	6.6 (5.9–7.4) 16,678	5.7 (5.0–6.5) 12,033	8.7 (5.5–13.6) 510	8.1 (6.0–10.8) 1,789	8.3 (6.2–10.9) 2,299	8.3 (6.7–10.2) 1,420

Other/questioning youth were statistically more likely to have been threatened or injured with a weapon on school property compared to heterosexual youth.

Table 6. Youth were bullied on school property during the 12 months before the survey

Sexual Identity Year	Total	Heterosexual (straight)	Gay or lesbian	Bisexual	Gay, lesbian, or bisexual	Other/Questioning
2021	15.0 (14.1–15.8) 16,706	12.0 (11.1–12.9) 12,059	26.4 (21.4–32.2) 509	24.4 (20.9–28.4) 1,791	24.9 (21.9–28.1) 2,300	21.1 (18.4–24.1) 1,431

All sexual minority groups were statistically more likely to have been bullied on school property compared to heterosexual youth.

Table 7. Did not go to school because they felt unsafe at school or on their way to or from school (on at least 1 day during the 30 days before the survey)

Sexual Identity Year	Total	Heterosexual (straight)	Gay or lesbian	Bisexual	Gay, lesbian, or bisexual	Other/Questioning
2021	8.6 (7.6–9.7) 17,110	6.6 (5.8–7.6) 12,341	13.2 (9.3–18.5) 518	14.4 (11.8–17.4) 1,836	14.1 (11.9–16.7) 2,354	12.6 (10.7–14.7) 1,467

All sexual minority groups were statistically more likely to not go to school because they felt unsafe at school or traveling to or from school compared to heterosexual youth.

Table 8. Were ever physically forced to have sexual intercourse (when they did not want to)

Sexual Identity Year	Total	Heterosexual (straight)	Gay or lesbian	Bisexual	Gay, lesbian, or bisexual	Other/Questioning
2021	8.5 (7.6–9.4) 14,158	5.0 (4.3–5.8) 10,230	16.9 (12.7–22.2) 418	23.3 (20.5–26.3) 1,509	21.9 (19.6–24.4) 1,927	15.9 (12.8–19.6) 1,2

 All sexual minority groups were statistically more likely to have been physically forced to have sexual intercourse compared to heterosexual youth.

Discussion

  According to one study from 2017 to 2020: the rate of violent victimization of lesbian or gay persons (43.5 victimizations per 1,000 persons age 16 or older) was more than two times the rate for straight persons (19.0 per 1,000); the rate of violent victimization against transgender persons (51.5 victimizations per 1,000 persons age 16 or older) was 2.5 times the rate among cisgender persons (20.5 per 1,000). In addition, only 58% of violent victimizations of lesbian or gay persons were reported to police. Furthermore, domestic violence was eight times as high among bisexual persons (32.3 victimizations per 1,000 persons age 16 or older) and more than twice as high among lesbian or gay persons (10.3 per 1,000) as it was among straight persons (4.2 per 1,000)." (Truman and Morgan) The previous research is in line with this study findings. In this study, all sexual minority groups were statistically more likely to have been electronically bullied compared to heterosexual youth. In addition, All sexual minority groups were statistically more likely to have been bullied on school property compared to heterosexual youth.
All sexual minority groups were statistically more likely to not go to school because they felt unsafe at school or traveling to or from school compared to heterosexual youth.
All sexual minority groups were statistically more likely to have been physically forced to have sexual intercourse compared to heterosexual youth.
  Bisexual youth reported highest percentage (5.4%) that they were in a physical fight at school. No statistically significant differences by sexual identity were found for physical fighting at school. Bisexual youth reported highest percentage (28.4%) of electronic bullying.

Other/questioning youth (8.3%) were statistically more likely to have been threatened or injured with a weapon on school property compared to heterosexual youth (5.7%). All sexual minority groups were statistically more likely to have been electronically bullied compared to heterosexual youth. This is consistent with previous research. (Ybarra, M.; Goodman, K.; Saewyc, E.; Scheer, J.; et al.)

Bullying prevention efforts should take into account that bisexual youth and other sexual minority youth have reported bullying more than heterosexual youth.

Sexual minority groups appear to be an important group for prevention and reduction of violence and injuries in youth. All sexual minority groups (21%-26%) were statistically more likely to have been bullied on school property compared to heterosexual youth (12%). All sexual minority groups (13%-14%) were statistically more likely to not go to school because they felt unsafe at school or traveling to or from school compared to heterosexual youth 6.6%. All sexual minority groups (16%-23%) were statistically more likely to have been physically forced to have sexual intercourse compared to heterosexual youth (5%). These findings are consistent with other studies that sexual minority youth experience more violence, threat or injury with a weapon, forced sexual intercourse, and bullying than heterosexual youth. (Haelle) (Inwards-Breland) (Miller) (Ybarra, M.; Goodman, K.; Saewyc, E.; Scheer, J.; et al.)

In prevention efforts, implementing effective prevention strategies, such as using seat belts , reducing the use of alcohol, using safety equipment and implementing injury prevention strategies will all contribute to reducing unintentional injuries. (Ballesteros, M; Williams, D.; Mack, K.; Simon, T.; et al.) Prevention opportunities extend beyond addressing individual risk behaviors to include programs, policies, and strategies that enhance protective factors within the family, schools, neighborhood, and community. "The frequency, severity, and potential for death and disability of these injuries together with the high success potential for prevention, make injury prevention a key public health goal to improve child and adolescent health in the future. ." (Ballesteros, M; Williams, D.; Mack, K.; Simon, T.; et al.)

School based intervention programs for injury and violence needs to identify and provide appropriates services for at risk youth. Guidelines include recommendations related to the following aspects of school health efforts to prevent unintentional injury, violence, and suicide: a social environment that promotes safety; a safe physical environment; health education curricula and instruction; safe physical education, sports and recreational activities; health, counseling, psychological, and social services for students; appropriate crisis and emergency response; involvement of families and communities; and staff development." (Barrios, Sleet and Mercy) Schools have a responsibility "to prevent injuries from occurring on school property and In addition, schools can teach students the skills needed to promote safety and prevent unintentional injuries, violence, and suicide while at home, at work, at play, in the community, and throughout their lives. The school health recommendations for preventing unintentional injury, violence, and suicide summarized here were developed by the Centers for Disease Control and Prevention [CDC] in collaboration with experts from universities and from national, federal, state, local, and voluntary agencies and organizations." (Barrios, Sleet and Mercy)

Further research needs to be conducted in bullying, violence prevention and unintentional injuries and impact on sexual minority youth given the fact that in general these youth are reporting higher vulnerability than heterosexual youth.

Sixty-five percent of states required teaching of violence prevention in middle and high schools, and there is little information available on whether or how often evidence-based curricula are used. (Schwarz, S) Despite evidence that preventive counseling from a clinician improves seat belt and helmet use and decreases use of illegal substances and other high-risk behaviors among adolescents, few clinicians provide such counseling. (Schwarz, S) Based on this research there is a strong need to fund programs that foster improved decision-making skills and provide positive models to reduce risk-taking behaviors that often lead to violence and injury. Also, there is a need to provide funding to replicate school-based health centers throughout the state, particularly those that provide mental health, behavioral health, and counseling services. Finally, need to pass legislation to support empirically proven strategies to reduce risky and dangerous (Schwarz, S) Schools should prioritize the development of anti-violence and anti-injury programs to improve health in their young adolescent populations.

Methods

Statistical analysis was performed on YRBS data imported into Epi Info 7 using procedures that accommodate the weighted sampling design of YRBS. YRBS is used to monitor priority health risk behaviors among youth in the United States. The national Youth Risk Behavior Survey (YRBS) uses a three-stage cluster sample design to produce a representative sample of 9th through 12th grade students. National data in YRBS High school student survey for 2021 were used to analyze the data. Baseline statistics were carried out and used chi- square to test for differences. Statistical analysis was carried out using Epi Info 7 software. Sexual identity groups were controlled for in the study and odds ratios were calculated for subgroups.

Acknowledgements

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Assessment of Carbon Capture Techniques and their Carbon Sequestration Potential, Technical Characteristics, and Cost By Connor Yu

Abstract

The scientific community has declared a need for urgent action on climate change to limit global warming to 1.5℃. To achieve this goal, carbon capture has been identified as a potential critical method. Currently, carbon capture facilities sequester around 45 megatonnes of CO_2 a year. The International Energy Agency estimates that around 1.2 gigatonnes of CO_2 must be removed by the year 2030 to stabilize the rate of global warming. This review compares the technical aspects, costs, and carbon sequestration potential of three carbon capture methods: direct air capture, biochar, and enhanced rock weathering. While direct air capture is the most developed and most reliable in sequestration ability of the three, it is more expensive than enhanced rock weathering and biochar, which are cheaper but more variable in sequestration. [1-2 summarizing sentences to drive home your findings from the review..]For these reasons, DAC is the frontrunner of carbon capture and holds the most potential in helping reach the 1.2Gt Target.

Introduction

The Intergovernmental Panel on Climate Change (IPCC) estimates that to keep the climate stable, global temperature rises must be limited to 1.5℃ annually (IPCC, 2018). The IPCC report predicts that if global warming exceeds this threshold, consequences could be irreversible: ecosystems could be lost, temperature extremes could increase, and sea levels could rise higher than if limited to 1.5℃ annually (IPCC, 2018).

While fluctuations in climate are considered natural phenomena, temperatures have risen dramatically due to increased emissions of greenhouse gasses by humans (NOAA, 2023). For millennia, atmospheric CO_2 concentrations have never exceeded 300 parts per million (ppm). However, in the last 200 years, CO_2 concentrations have increased by 50% to 422 ppm (NASA, 2023). This has raised the Earth's average temperature by 2°F since 1880, resulting in more frequent regional and seasonal temperature extremes (NOAA, 2023).

To achieve the goal of limiting global warming to 1.5℃, the IPCC projects that emissions must reach "net zero", or a state in which greenhouse gasses emitted to the atmosphere from human activities are balanced by removal of these gases from the atmosphere, by the year 2050 (IPCC, 2022). These gasses can be removed through carbon sequestration; the process of transporting CO_2 from the atmosphere into global pools such as oceans and geological strata (Lal, 2007).The IEA projects that to reach this goal, in addition to renewable energy, around 1.2 gigatons (Gt) of carbon dioxide (CO_2) must be captured each year (IEA, 2023). This is the same amount of CO_2 that 6.4 billion acres of forests remove annually (EPA, 2023). This amount must be removed through carbon capture and storage (CCS), where certain processes remove CO_2 from the atmosphere and then store it away either underground or in oceans (Tahmasebi et al., 2020).

This review assesses three different types of carbon capture methods at varying stages of development: Direct Air Capture (DAC), Biochar, and Enhanced Rock Weathering (ERW). DAC involves the extraction of CO_2 directly from the air, usually using one of two types of materials: liquid solvents or solid sorbents. Both materials react with and trap CO_2. These materials are heated up, releasing CO_2, which is stored away permanently in a storage facility (McQueen et al., 2020). Biochar, as defined by the International Biochar Initiative, is "a solid material obtained from the carbonization thermochemical conversion of biomass in an oxygen-limited environments" (IBI, 2022). iochar can be composed of many different biomass sources, including food and plant waste. Because biochar stores CO_2, it does not require external storage and can be added to soil (cite). Similarly, ERW also does not require external storage, but instead has to process materials. This involves applying rocks rich in calcium and magnesium to soil to speed up the carbon removal process as the rocks naturally weather and react with CO_2 in the air (Beerling et al., 2020). This review evaluates DAC, biochar, and ERW's potential to sequester carbon and consequently, their relevant economic and technical concerns.

1). Carbon Sequestration Potential
1.1 Direct air capture

Direct air capture involves the use of either solid or liquid sorbents to directly absorb CO_2 from the atmosphere (Fig. 1). After outside air is blown into contact with the sorbents, the filters are heated at low heat for an extended period of time to release the CO_2, which can then be stored away or reused for industries like the carbonated beverages industry.
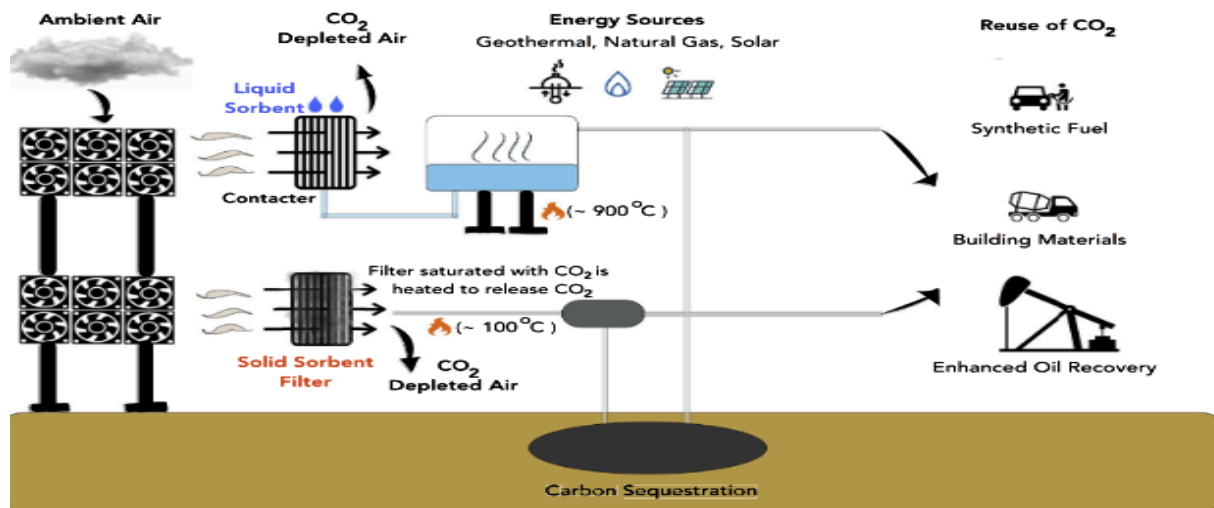
Figure 1. Direct Air Capture Process (Ozkan et al., 2022)

As of 2023, around 27 DAC plants are active, with six new plants under construction, capturing about 0.01 megatonnes (Mt) CO_2 per year (IEA, 2023). A recent systematic review found that the carbon sequestration potential for DAC is 0.5–5 Gt CO_2 per year, which is the equivalent of the CO_2 sequestered by 6 million to 6 billion acres of forests (Fuss et al., 2017; EPA, 2023). While the sequestration potential of DAC as a whole is often understood to be

unlimited due to DAC's stable sequestration rate, DAC is held back by high sorbent costs and technical considerations, mainly storage (Fuss et al., 2017).

Sabatino et al. (2021) found a difference between solid and liquid sorbents and the amount of CO_2 captured over time per unit of sorbent volume, or "productivity". They found lower ranges of productivity for liquid-solvent processes than solid sorbent processes due to . Additionally, there was a distinction found between different types of compounds: physisorbents, which are based on crystalline compounds consisting of metal ions, and chemisorbents, which are based on amines (Leonzio et al., 2022). Leonzio et al. (2022) found physisorbents were not only more expensive and less energy efficient than the chemisorbents, but they also sequestered less CO_2 (Leonzio et al., 2022). DAC plants using physisorbents also had lower sequestration results than chemisorbent-using ones due to the higher amount of sorbent needed and higher energy costs (Leonzio et al., 2022).

Many studies do not consider storage or transportation of CO2 aspects, despite this being the main limitation of DAC. (Sabatino et al., 2021). While in the US, there is enough storage space to easily store trillions of tons of CO_2, these spaces are not developed enough (DOE, 2023). Additionally, a study found that CO_2 storage underground in depleted oil and gas fields is not readily available for commercial scale (Bui et al., 2018). Overall, DAC's high sequestration rate makes it very promising for reaching "net zero", but its efficacy depends on the type of sorbent used and the availability of storage.

1.2 Biochar

While DAC requires external storage of CO_2, biochar itself stores carbon. Biomass undergoes carbonization, usually through pyrolysis, or the process of transforming a material by heating it to a very high temperature in the absence of oxygen (Tam & Bhatnagar, 2016). Thus, biochar can be made from many different sources of biomass, making the process very practical.

Although there are several sources of solid biomass for biochar, different feedstocks, or the raw materials used, can affect the sequestration potential (Yargicoglu et al., 2015; Ahmed et al., 2007; Masek et al., 2018). Specifically, feedstock consisting of woody biomass was found to produce biochar suited for sequestration purposes, having higher amounts of fixed carbon (Yargicoglu et al., 2015). Biochar made from the date palm leaf could sequester up to 25% of the CO_2 inside of a closed container in addition to the carbon stored inside the biochar itself (Salem et al., 2021).

A challenge of relying on biochar for carbon sequestration is the inconsistency in sequestration that comes from using different materials. Sadasivam & Reddy (2015) found that the physical and chemical properties of biochar "significantly impacted" the sequestration potential of greenhouse gases, with certain materials unable to adsorb as much. Even among specific types of biochar, including those derived from wood, sequestration potentials varied wildly (Yargicoglu et al., 2015). Biochar's quality can also be affected by the uniformity of the feedstock, the type of pyrolysis process used and any carbon losses from the biomass before it enters pyrolysis (Masek et al., 2018). To address these concerns, the UK Biochar Research

Centre (UKBRC) developed a set of standard biochar materials, known as the Edinburgh Standard Biochar set, which were made freely available to research groups around the world (Masek et al., 2018). Masek et al. (2018) found that when using these materials, different types of pyrolysis units were able to produce similar biochar with consistent quality parameters, albeit not at an industrial scale. Biochar's inconsistency in its carbon sequestration rate remains its largest obstacle to its adoption on a large scale.

1.3 Enhanced rock weathering

ERW also suffers from a lack of consistency arising from the materials used. However, unlike biochar, the rocks do not store carbon, rather they accelerate the natural weathering process. After the rocks are mined, they are ground into fine particles to increase their surface area, which speeds up the weathering reaction. These particles are spread on land, usually cropland. Next, the CO_2 in the atmosphere combines with rainwater and forms carbolic acid (Fig. 2). This acid reacts with the rocks scattered on the field, forming solid carbonates, which are then washed into the sea for storage in the ocean.

How enhanced rock weathering works
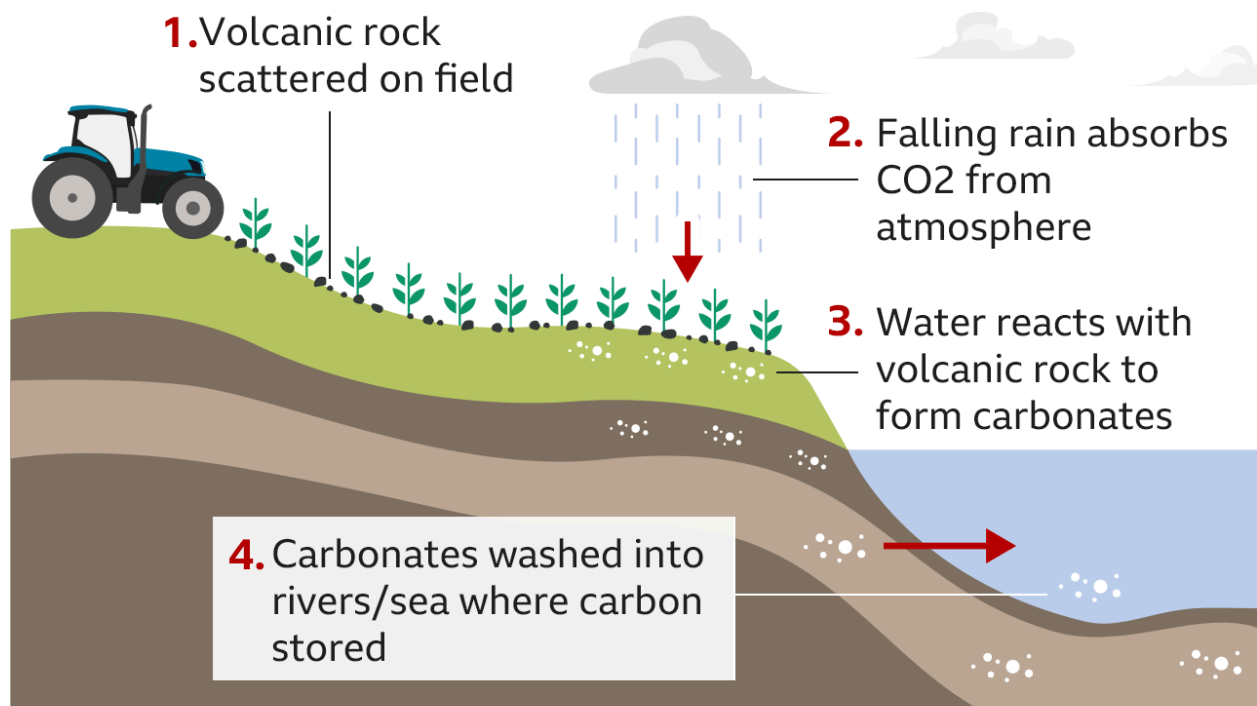
Figure 2**.**
How enhanced rock weathering works (BBC, 2023).

The most common rock used for ERW is basalt, however other studies have used dunite and olivine (Strefler et al., 2018; Garcia et al., 2020; Rigopoulos et al., 2018). Strefler et al.

(2018) found global sequestration potentials of 4.9 Gt of CO_2 annually for basalt and 95 Gt of CO_2 annually for olivine. While these rocks are relatively good at sequestering CO_2, the main issue for its carbon sequestration potential is that the mining, processing, and transportation all emit CO_2, effectively lowering the net sequestration of ERW. Ioannis et al. (2017) found that the processing of the rock into fine particles could reduce the overall sequestration of ERW by 30%, and the mining required could reduce it by an additional 0.1-1%.

2). Costs / Technical concerns

These three technologies have a wide range of costs and technical concerns. DAC is the most expensive and energy-intensive technology, but is also the most developed in terms of sequestration potential. Biochar is much cheaper, but its effect on soil has not been thoroughly researched. ERW is more expensive, but has a lower range of technical concerns.

2.1 Direct Air Capture:

DAC, the most expensive of the three, has the fewest technical challenges. Unlike ERW or biochar, DAC's sole purpose is carbon capture, so its environmental impacts are usually neglected or assumed to be minimal (Ozkan et al., 2022; McQueen et al. 2021). The main barrier to DAC's use is its cost. A study by Bui et al. (2018) estimated DAC's costs to be in the $600-1000 range per ton of CO_2. The bulk of this cost comes from purchasing sorbents, with it being estimated that sorbents consist of around 80% of the total annual capital cost of a DAC plant (McQueen et al. 2020). While scientists generally agree more research needs to be done on the sorbents themselves, they have also found a variety of other ways to decrease DAC's cost (Ozkan et al., 2022; McQueen *et al.,*2021). McQueen et al. (2021) suggests that DAC's cost could naturally decrease through a learning curve or learning by doing, in which research and development advance the technology and lower costs. Additional reductions could come from cost subsidies, which the US currently has in the form of tax breaks for any DAC facility that removes at least 100 kilotons of CO_2 per year (McQueen et al., 2020).

The other major barrier to DAC's adoption is its energy requirements and the associated cost. DAC requires a specific ratio, around 80% thermal energy and 20% electricity (McQueen et al., 2020, McQueen et al.*,* 2021). Ozkan et al. (2022) estimated the energy required for DAC is 6.57-9.9 gigajoules (GJ)to capture a ton of CO_2 for liquid processes and 3.5-6.6 GJ for solids . This is the same amount of energy produced by around 170-257 liters of gasoline (FortisBC, 2023). This higher energy cost means that renewables would have to be used to power DAC, otherwise the fossil fuels used could release more than half the CO_2 captured by DAC (Ozkan et al., 2022).

To decrease these energy requirements, scientists have tried a variety of approaches. Ozkan et al. (2022) showed that solid sorbents require less energy per ton of CO_2 sequestered. Per ton, solid sorbents required between 32% and 44% less energy for heating. Additionally, using heating, ventilation, and air conditioning (HVAC) systems to recirculate heat could substantially reduce energy consumption. Baus and Nehr (2022) found that it reduced the energy

demand of a building by 37%. This drastic reduction could give DAC a unique use in improving indoor air quality. DAC remains the main sequestration option even with these concerns.

2.2 Biochar

Biochar, while cheaper than DAC, has varying costs and under-explored impacts on the land it is applied to. While using waste biomass can be very cheap, using virgin, or pure, biomass can raise the costs to over $120 per ton of CO_2 sequestered (Shackley et al., 2014). For waste biomass, costs still vary, but by less. Shackley et al. (2014) found costs of around $27 per ton of green waste, $61 per ton of wood waste, $43 per ton of food waste, and $55 per ton of sewage. Additional costs can come from transportation and application of biochar. Despite this, biochar remains significantly cheaper than DAC.

Biochar's main issue comes from its effects on the land. There have been few long-term studies on biochar and many of its effects are undocumented (Shackley et al., 2014, Gross et al., 2021, Ahmed et al., 2007). While biochar's impacts are likely to be positive for the environment, a great deal of uncertainty surrounds these impacts (Xie et al., 2015; Palansooriya et al., 2019; Dickinson et al., 2014). Biochar's impact on soil productivity, water quality, or even the general environment have yet to be measured (Ahmed et al., 2007, Shackley et al., 2014). Because of this, it becomes very difficult to extrapolate what kind of large scale effects could have on the environment. Due to these blind spots, biochar's safety as a carbon capture method is questionable.

While biochar is very cheap, its properties may not be worth the cost. The benefits of biochar for agriculture are modest at best, and the lack of understanding around biochar makes it risky to use. Dickinson et al. (2014) found that, combined with biochar's cost, its limited benefits make biochar a relatively poor option for cereal farmers. Biochar's merits outside of carbon capture are limited, lowering its potential as a general product.

2.3 ERW

ERW acts as a middle ground between DAC and biochar. While not nearly as cheap as biochar, ERW's effects on the environment are well documented, with fewer variables to account for. Unlike biochar, ERW's difference in its costs for different materials stems purely from sequestration potential, with it costing around $60 to sequester a ton of CO_2 with dunite and $200 with basalt (Strefler et al., 2018). This cost can vary depending on the distance transported, processing time, and electricity prices for mining and crushing. Strefler et al. (2018) maintains that while these costs are high, ERW could become more competitive if its benefits to the soil or nutrient supply are taken into account.

Other than sequestration, ERW has a variety of benefits to the environment. Basalt particles can increase soil pH, replenish nutrients, and even potentially protect against droughts (Garcia et al., 2019). These benefits make it incredibly useful for farmers, and even a possible substitute for industrial fertilizers. Additionally, ERW has the potential to fight another effect of climate change: ocean acidification (Rigopoulos et al., 2018, Strefler et al., 2018). Seawater

normally has an average pH of 8.2, but since the Industrial Revolution, the average pH has decreased to 8.1 pH, which is an acidity increase 100 times greater than any natural rise seen over millions of years (WHOI, 2023). Higher CO_2 levels are to blame for this increase, with more carbolic acid being formed as the ocean absorbs more CO_2. These additional benefits make ERW very appealing as a carbon capture method.

ERW's main challenges come not from its price, but the scale of mining and processing needed for the process to be scaled up. Strefler et al. (2018) found that it takes around 3 Gt of basalt to sequester one gigaton of CO_2, which, while technically feasible due to being below global coal production, would still require a large amount of mining. Additionally, the processing required for ERW to function on a large scale could also cause severe wearing of milling equipment, which would decrease efficiency (Haug et al., 2010). Overall, ERW remains a strong sequestration option, but requires optimization of mining, processing, and transportation as well as further research on its effects on the land.

3. Conclusion

To combat climate change, carbon capture technologies will be instrumental in keeping global temperature raises under two degrees Celsius. Three of the main carbon capture technologies, DAC, biochar, ERW, have been considered in this review. DAC benefits from consistency in its sequestration potential but is held back by high costs, lack of consensus on storage, and energy requirements. Biochar, on the other hand, has lower costs but higher uncertainty in its sequestration efficiency and environmental impacts. ERW is expensive but has lower costs than DAC, is more reliable as a carbon capture method than biochar, but is held back by the scale of mining and processing needed if ERW becomes widely used. Prioritizing direct air capture could be most successful in reaching the 1.2Gt target, given that its issues are not fundamentally with the technology itself, but rather the cost and energy intensity of the process. Additionally, DAC is by far the most developed technology, with it being the only technology that is currently supported by subsidies in the US. For these reasons, DAC is the frontrunner of carbon capture and holds the most potential in helping reach the 1.2Gt Target.

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The Willingness of Korean-American Adolescents to Maintain Their Heritage Language and Culture By Claire Bahk

Introduction

Since its formation, the United States has experienced a large amount of immigration from various Asian nations, including Korea. The first wave of Korean immigration to the U.S. began in 1903 when immigrants arrived in Hawaii by ship in order to escape famine and political turmoil (Koo and Yu 2). The struggles during and after the Korean War triggered the second wave of immigration, mainly consisting of Korean wives of American soldiers, collectively known as "war brides" (Chung). After the 1965 Immigration and Naturalization Act abolished the national origins quota system, which limited the number of immigrants entering the U.S., the third wave of Koreans arrived in search of educational and career opportunities (Chung). Today, the U.S. has the largest South Korean population in the world outside of the Korean peninsula itself (Esterline and Batalova).

Korean immigrants migrate from a country that is regarded as "one of the most linguistically and ethnically homogenous countries in the world" (Han 13). This fact speaks to the difficulty of assimilation and acculturation that Koreans can experience in a predominantly white, English-speaking country. Yet, many Koreans fight against assimilating, as they consider preserving their language and traditions critical. To support this belief, several studies have found that Korean-immigrant parents often strongly compel their children to retain the language, such as Mihyon Jeon's 2008 study "Korean Heritage Language Maintenance and Language Ideology". However, there is a significant number of Koreans who prefer to assimilate into American culture, and most begin this process by becoming proficient in English. Heekyung Han(2011), researcher at the University of Illinois at Urbana-Champaign, credits three factors that have contributed to this desire among Koreans, which he has coined "English fever." The first is called *Sekehwa*, or the process of national globalization. This occurred as Koreans participated in the 1986 Asian Games and the 1988 Olympics held in Seoul and experienced the 1997-1998 Korean Financial Crisis. These major events prompted Koreans to recognize the importance of English proficiency. Another factor occurred in 1991, when the Korean government required all elementary schools to teach English by 1995 (Han 11). The third cause occurred when Korean educational experts urged for the teaching of the English language to move its focus from grammar and vocabulary memorization to real-life communication skills (Han 11). In addition to these factors, scholars and educators are considered to be among some of the elite professions within Asian societies, and education is considered crucial for "family glory and status" (Choi and Kim). Hence, the given emphasis on education and proficiency in speaking English is extremely prevalent and strong among Koreans.

The preference for assimilation leads to a phenomenon known as subtractive bilingualism: the process by which one learns a second language at the expense of his or her first (Fillmore 323). As subtractive bilingualism continues to impact the Korean community in

the U.S., the discussion surrounding the retention of the Korean language and culture in America is increasing in importance. The current body of literature on this topic is limited to studies focused on the perspectives of Korean parents and simple correlations between one's Korean proficiency and cultural connection. However, as adolescents are the ones who will define future generations of Korean-Americans, it is pertinent to close this gap by discovering the perspectives of Korean-American adolescents on the maintenance of their heritage language and culture and which factors contribute.

Literature Review

Before investigating the perspectives of Korean-American adolescents, it is necessary to gain a solid grasp on the current understanding by examining the existing body of research. Heritage language and culture maintenance has been the subject of many studies during the course of the past century. In light of California's English-only policy in the late 1990s, a significant number of studies have stressed the importance of preserving heritage languages and culture. California legislators expressed concern that immigrants were not assimilating quickly enough because the bilingual education system implemented at the time eliminated the necessity to learn English (Lee 327). As a result, Proposition 227 was passed in 1998 and required public schools in California to conduct instruction "overwhelmingly" in English. (McCloskey et al. 3).

Various other studies were conducted in response to California's new legislation regarding Korean immigrants. Lily Wong Fillmore of the University of California, Berkeley and her colleagues conducted a national survey of language-minority families with children who attended preschool programs which were held either entirely or partly in English (333). Their survey, in which 13.6% of the family participants were Asian, investigated the extent to which these programs were affecting the children's language patterns. It was found that 64.4% of the Asian families whose children attended entirely English-only preschool reported that the home language was displaced by English (Fillmore 333). Also responding to Proposition 227, researcher Steven K. Lee of California State University administered a questionnaire to a group of students with Chinese and Korean heritage in order to determine the significance of language and cultural orientation to academic achievement (327). In addition, he looked for any relationship between academic achievement and the level of interest in maintaining their heritage language and culture. His study found that students "who had a greater awareness for, and interest in, developing biculturalism had superior grade point average than their counterparts who had less interest in their heritage," with Lee noting that the correlation was "very significant" (333).

There also has been an extensive body of research regarding the perspectives of Korean parents on heritage linguistic and cultural maintenance. Han studied participants from a Korean language school in Champaign county, Illinois and found that the majority of Korean parents chose developing literacy skills as the most important reason for sending their children to Korean language school (45). He also found that many Korean immigrant parents stated that

strengthening their children's Korean identity to be an important reason (Han 45-46). This adherence to heritage language and culture was also demonstrated in a study by University of Pittsburgh researcher Yunjin Oh and colleagues. The researchers distributed a cross-sectional survey from 157 Korean immigrants residing in the Pittsburgh, Pennsylvania, area. Their study showed that Korean-educated respondents, who likely resided in Korea for a longer time than those who were not Korean-educated, were more likely to resist adopting a U.S. identity (Oh et al. 524). This demonstrates that they had a closer connection to Korean language and culture that caused a stronger reluctance to lose some of their Korean heritage and assimilate into American culture, hence a reason for insisting their children do the same.

Other research has provided further insight regarding Korean-Americans and their Korean heritage. Adam Winsler of George Mason University and colleagues conducted a study of families with the heritages of or from the countries of Mexico, Puerto Rico, Cuba, India, China, Japan, Korea, and Vietnam. Participating families had collectively 9,250 children (Winsler et al. 752). The researchers found that "Korean American families show stronger cultural homogeneity and adherence to the norms and practices of their indigenous culture" (Winsler et al. 752). However, contrary to this, Winsler found that Korean families were also among those with the lowest rates of speaking a language other than English at home (752).

Many other studies have drawn similar conclusions. Mihyon Jeon of York University interviewed Korean-Americans to assess their attitudes toward language maintenance. One participant, Mike, recalled that his parents had never taught him Korean and only spoke to him in English due to their fear of him falling behind in school in America (Jeon 213). Another participant, Mrs. Park, described her concern with her husband's demanding and violent attitude towards his children regarding their learning of English (Jeon 212). Mrs. Park told Jeon that her husband even eliminated all traces of Korean from their home (212). Jeon surmised that this may be due to a feeling of vulnerability as Koreans residing in the U.S. and viewing themselves as having a lower status due to their inability to speak the dominant language fluently. To support this notion that some Korean parents prioritize assimilation, Hyun-Sook Kang of Illinois State University stated from his own research that more and more Koreans are moving to the U.S. to secure their children's education in American schools (250).

Research has shown that the behaviors and opinions of Korean parents affect their children's desires to continue to preserve their Korean language and culture. Grace Cho, professor and chair of the Department of Secondary Education at California State University, Fullerton, writes that "parents are perhaps the most significant HL [heritage language] provider for immigrant children and have the ability to compensate for the lack of access to the HL outside of the home" (36). Parents therefore possess the powerful ability to control the exposure their children have to their respective heritage language. Those who wish for their children to preserve the heritage language and culture will presumably place more emphasis on both and give more exposure to their children than those who do not. Many researchers have also corroborated intergenerational transmission of heritage language to be an extremely effective way of preserving a language and found that a parent's use of heritage language with his or her

child is crucial to language preservation (Cho 36). Furthermore, in her research, Hanna Kim of the University of Mississippi found that children whose parents forced them to use their native language at home believed that their parent's discipline was a deciding factor for them to maintain their Korean language proficiency (43).

Other findings from as long as 50 years ago have also identified factors that may influence the ability to speak Korean and the choice of retaining Korean language and culture. Cho detailed the idea of heritage language competence, citing two studies that both found an inverse relationship between English and heritage language competence; when English proficiency increased, the heritage language proficiency decreased and vice versa. One of those studies was conducted by Min Zhou in 2001 of Vietnamese teenagers which found that after two years of living in the U.S., 61% reported a decline in heritage language competence that was coupled by an increase in English proficiency (Cho 30). The second study was done in 1983 by Barbara J. Merino of Spanish speakers and reached similar conclusions (Cho 30). These findings from participants of various ethnic backgrounds may hold true for Korean immigrants, as well.

Korean churches have also been found to play a crucial role in preserving Korean culture among Korean-Americans. Korean churches in the U.S. first developed as centers for the Korean independence movement during the Japanese occupation of Korea, but have advanced to be gathering centers where Korean immigrants participate in cultural practices and celebrate traditional holidays (Min 1382). Korean churches frequently provide language programs as well—"Nearly half of the Korean churches in New York City have established a Korean language program" (Min 1383). Churches also provide a space for social interactions among Koreans, increasing opportunities for them to speak the language and practice the culture. Kim found that the significant majority of those who attended Korean churches reported that they enabled them to create social networks with fellow Koreans and feel a greater connection to their ethnic culture (44).

The retention of heritage language and culture has been shown to affect identity and mental health. According to Andrew Fuligni and Janet Oh of the Department of Psychology at California State University, limited proficiency of heritage language has been linked to feelings of isolation, impacting the development of one's ethnic identity (204). They found that acculturation in regards to the English language increased depression in Korean-Americans due to it "eroding a sense of Korean identity and participation in traditional practices" (Oh and Fuligni 204). Similarly, in interviews with immigrant families, Fillmore demonstrated that many of them had difficulties with communicating.

For many families with immigrant parents, language barriers play a considerable role in interfamilial conflicts. As children begin to assimilate and predominantly speak English, many parents are unable to effectively communicate with their children due to disparities in English abilities (Fillmore 324). This can discourage interactions, hinder communication, and incite arguments or tension. In fact, Oh and Fuligni write, "Children's refusal to speak the HL [heritage language] can also be a constant source of tension between parents and children"

(204). For example, Mrs. P's younger children did not retain Vietnamese and experienced unpleasant interactions with their father as a result of impaired communication (Fillmore 339).

The aforementioned studies and the existing body of literature have provided insight into the perspectives of Korean parents on the maintenance of heritage language and culture. Existing research has also shed light on simple correlations that affect the retention of Korean heritage. However, there is a significant lack of knowledge on what factors affect Korean-American adolescents' desire or willingness to maintain the Korean language and culture. This leads to the research question, what factors influence Korean-American children of Korean immigrants between the ages of 13-18 in southeastern Michigan to maintain their heritage language and culture and to what extent? The researcher hypothesized that the majority of Korean-Americans are willing to maintain their native language and culture and that those whose parents have stronger preferences for maintenance will express stronger preferences, as well.

Methodology–Design

To determine Korean-American adolescents' levels of willingness towards maintaining the Korean language and culture and which factors affected this willingness, the researcher implemented a mixed methodology to identify a correlation between social and familial factors and individual willingness. After gaining permission from the school district's Institutional Review Board (see Appendix A), primary data was collected through surveys. The surveys were influenced by Su-Jin Sue Jung's "Social Capital and Cultural Identity for U.S. Korean Immigrant Families: Mothers' and Children's Perceptions of Korean Language Retention," which used narrative inquiry and semi-structured interviews to study the perceptions of and experience with maintaining the Korean language of Korean immigrant mothers and children in the U.S. This survey was designed to collect both quantitative data and qualitative data: quantitative data provided an objective perspective to identify overall trends and patterns in participants' attitudes and allow for generalizations, qualitative data was collected for additional explanation.

The chosen methodology is justified by other studies of the same topic with similar methods,such as the research by Joseph D. Hovey, Sheena E. Kim, and Laura D. Seligman of the University of Toronto, which studied the correlation between heritage language use among Korean-American college students and mental health through electronic surveys (502). Eun Joo Kim of Ohio State University also chose surveys to gather information on her study of Korean-English bilinguals' experiences learning Korean and English and the influence of the age at exposure to the second language on maintenance of Korean and English (244).

Participants

Participants were of Korean descent, between the ages of 14 and 18, and lived in southeastern Michigan. Participants were recruited through Korean language classes, Korean churches, traditional Korean music classes, Korean volunteer organizations, Korean and Asian

school clubs, and the researcher's network of personal acquaintances. After the initial stages of outreach through convenience sampling, snowball sampling was used to grow the sample size. After seeking out additional participants to make up for responses that were excluded due to inappropriate and irrelevant answers and people who were contacted but did not respond, a total of 48 responses were obtained, which exceeded the goal sample size of 30 responses.

Participation in the study was voluntary. Prior to taking the survey, participants were given a description of the study and were asked to give their consent and their parent's, if they were under the age of 18. Participants were made aware of their right to withdraw and that the survey was anonymous. Surveys were distributed to participants electronically and could be taken at a time and place most convenient for them.

Materials

A digital survey creator was used for writing and distributing the questionnaire. Respondents answered using their own personal electronic devices.

Procedure

The survey was distributed through Google Forms via link or QR code, and participants used their own digital devices - phones, computers, Chromebooks - to complete the survey electronically. The survey was tested with a small group before official distribution in order to verify its functionality and accuracy. The survey required approximately 15 minutes and consisted of 34 questions. In preparation for data analysis, the researcher removed all responses that were deemed incomplete, inappropriate, and irrelevant. In order to measure the varying levels of attitudes and behaviors towards maintaining the Korean language and culture, a 5-point Likert scale was applied on certain questions. A point value of 1 represented negative attitudes and behaviors towards language and culture retention, while a point of value of 5 represented positive attitudes and behaviors. Qualitative data was analyzed to identify themes and patterns among responses. Reliability was achieved due to consistent use of the same survey questions for all participants.

Limitations

Certain difficulties were present throughout the duration of collecting data: the restricted amount of time given to complete data collection and the specific criteria for participants significantly limited the sample size while also making it difficult to find participants who were eligible. In addition, some participants did not answer questions appropriately or provided completely irrelevant responses. Due to the researcher's Korean background and preference to maintain the Korean culture and language, there was a possibility for a biased interpretation of the open-ended questions. Despite these limitations, the researcher obtained valuable information from a significant number of participants that properly reflected the research question and contributed to the researcher's findings.

Results –Quantitative Results

       48 participants with varying demographics completed the survey. 50% of the 48 participants were male and 50% were female (see fig. 1), demonstrating a relatively fair representation of gender. Regarding age, all ages from 14 to 18 were represented: 8% of the total participants were 14, 13% were 15, 23% were 16, 33% were 17, and 23% were 18 (see fig. 2). The dominant majority, 94% of total participants, were of 100% Korean descent, meaning that both parents are full Korean. 2% were of 75% Korean descent and 4% were of 50% Korean descent (see fig. 3). Similarly, 92% of participants had parents who were both born in South Korea. 2% had only one parent born in South Korea and 6% had parents that were both not born in South Korea (see fig. 4).

Gender Distribution

Female 50.0%

Male 50.0%
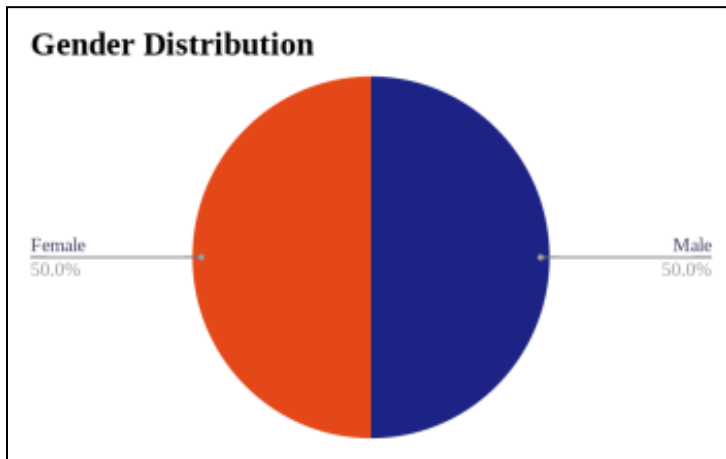
Fig. 1. Total Distribution of Gender Demographic

Age Distribution

18 22.9%

14 8.3%

15 12.5%

16 22.9%

17 33.3%
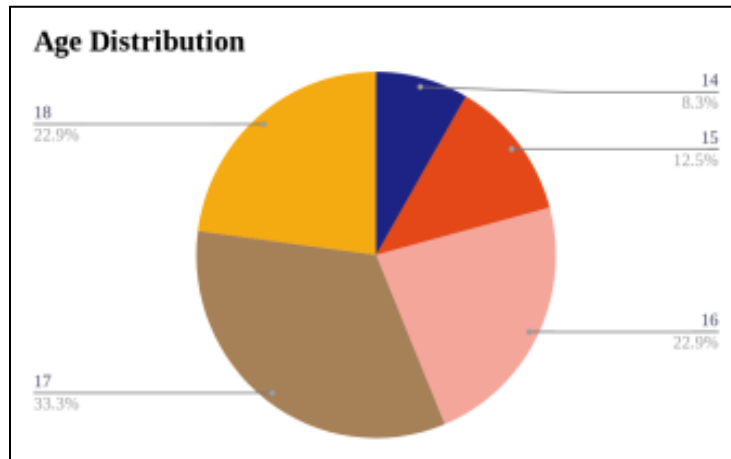
Gender. Per the responses gathered, gender was not a significant factor affecting the attitudes and behaviors of participants. For example, the percentage of those who speak Korean more often with their parents was the same for both genders (58%). Of those who speak Korean more often with their parents, the percentage of those who spoke Korean 90-100% of the time was 54% for males and 62% for females and the percentage of those who spoke Korean 75-89% of the time was 17% for both genders.

Age. Because only 4 and 6 participants were 14 and 15 years old respectively, the researcher determined that the sample size was not big enough to yield realistic and representative results. Hence, the effect of age was determined through the 79% of respondents that were either 16, 17, or 18 years old. The majority of these age groups stated that they believed maintaining the Korean language and culture was "somewhat important," "important," or "very important" (see tables 1 and 2).

Table 1
Importance of Maintaining Korean Culture

Likert Value	Age		
	16	17	18
1 (Very unimportant)	0%	0%	0%
2 (Unimportant)	0%	0%	0%
3 (Somewhat important)	36%	31%	18%
4 (Important)	18%	25%	27%
5 (Very Important)	45%	44%	55%

Table 2
Importance of Maintaining Korean Language

Likert Value	Age		
	16	17	18
1 (Very unimportant)	0%	6%	0%
2 (Unimportant)	18%	0%	9%
3 (Somewhat important)	27%	19%	27%
4 (Important)	18%	44%	9%

5 (Very Important)	36%	31%	55%

Parental Factors. An overwhelming majority of the 48 participants responded that their parents neither set consequences for not speaking Korean nor provide encouragement or incentives for speaking Korean (see fig. 5).

Fig. 5. Distribution of Parental Actions for Encouragement of Korean Language Use

Korean church. 92% of the total participants have attended or currently attend a Korean church. Of them, 91% reported having positive attitudes toward the maintenance of the Korean language and culture. The 8% who stated they did not have a church affiliation also reported having a positive attitude towards maintaining their Korean language and culture, as all these respondents stated that maintaining both the Korean language and culture was "very important" (see tables 3 and 4). Furthermore, when these respondents were asked whether they spoke Korean or English more often with their parents, all of them stated they spoke Korean with their parents for 90-100% of their interactions.

Table 3
Importance of Maintaining Korean Language

Likert Value	Korean Church Affiliation	
	Yes	No
1 (Very unimportant)	2%	0%
2 (Unimportant)	7%	0%
3 (Somewhat important)	25%	0%

4 (Important)	32%	0%
5 (Very Important)	34%	100%

Korean friends. There were varying percentages of respondents who spoke English or Korean with their parents among participants with different numbers of Korean friends. Of those who speak English most often with their parents, most had more than 15 Korean friends and the least had 11-15 Korean friends. Similarly, of those who speak Korean most often with their parents, most had more than 15 Korean friends, but the least had 1-5 Korean friends (see table 5). In addition, most participants who assigned a 5-point value for the importance of retaining Korean culture had 6-10 Korean friends.

Table 5

Correlation Between Korean Friends and Preferred Language With Parents

Number of Korean Friends	Language Spoken Most Often with Parents	
	English	Korean
1-5	43%	57%
6-10	25%	75%
10-15	25%	75%
15+	40%	60^

Table 6

Correlation Between Korean Friends and Designated Importance to Retain Korean Culture

Number of Korean Friends	Likert Point Value Assigned				
	1	2	3	4	5
1-5	0%	0%	50%	25%	25%
6-10	0%	0%	13%	13	75%
10-15	0%	0%	33%	33%	33%
15+	0%	0%	22%	33%	44%

Qualitative Results

        The researcher organized individual responses into distinct patterns in attitudes and behaviors.

        28. If you speak any Korean with your parents, please describe your experiences when you communicate with your parents in Korean? 54% of total participants shared an easy, comfortable, and good experience speaking Korean. 17% expressed that speaking Korean was just considered normal. 15% described experiences of miscommunication and difficulties finding the right words. Another 15% shared that they used a mix of both Korean and English to communicate with their parents.

        29. How do your parents support your Korean language learning, if applicable. Please give an example. 38% of total participants stated that their parents sent them to Korean school or encouraged involvement in its events, such as volunteering. 40% characterized their parents' support as conversational: the parents carry out conversations in Korean while correcting any pronunciation or grammar mistakes. 8% stated that they received study material, such as books or videos, from their parents and 15% reported no support from their parents.

        30. When you think about who you are, do you see yourself as Korean or American? Why? 44% of total respondents identified themselves as Korean, 27% identified as Americans, and 29% identified as both. Those who identified themselves as Korean cited reasons such as being born in Korea, being of Korean descent, having Korean citizenship, and being part of the culture and heritage. Those who identified themselves as American contributed their decision to cultural familiarity, prolonged time spent in the U.S., and being born in the U.S.

        32. Why do you speak Korean? 38% of total participants attributed their usage of Korean to it being their native language. 40% linked communication with family and friends to be the reason why they speak Korean. 23% cited culture as the main reason.

        33. In the future, do you want to continue to learn the Korean language? Why or why not? 94% of the total participants expressed a desire to continue to learn the Korean language, while 6% expressed the opposite wish. Those who wanted the former gave reasons such as communicating with family, connection to culture and heritage, respect for family history, and passing on to future generations.

        34. In the future, do you want to continue to participate in Korean culture? Why or why not? All participants expressed a wish to continue to participate in Korean culture, though of varying degrees. The two main themes identified were cultural identity and Korean food.

Discussion

        This study explored the effects of social and familial factors on the level of willingness of Korean-American adolescents to maintain the Korean culture and language. Results demonstrated that most Korean-American adolescents show a generally positive preference towards maintaining both the Korean culture and language, confirming my hypothesis.

        Although it was not accounted for in my hypothesis, age was identified as a significant factor that demonstrated a positive correlation with levels of willingness. Besides a single

outlier, older adolescents designated greater importance on retaining the Korean culture and language - the 18-year-old age group had the highest percentage of respondents who designated a Likert value of 5 (very important) for their perceived importance of maintaining the Korean language and culture. This may be attributed to the fact that older adolescents are more likely to realize the importance of speaking a second language, as it can benefit them in educational and career opportunities. In addition, older adolescents may possess more maturity to prioritize communication with their families and peers of the same ethnic background. In fact, of all 18-year-old respondents who designated either a Likert value of 3, 4, or 5 for their designation of importance for retaining the Korean language and culture, the percentage that cited communication with family to be the reason why they would like to maintain the language and culture was 67% and 44% respectively.

Unlike age, the only factor that had a strong correlation with the levels of willingness expressed by Korean-American adolescents, many factors were identified as having no significant correlation. For example, parental factors were not determined to be a predictor of increased levels of willingness. While 58% of respondents used mostly Korean to communicate with their parents, nearly all participants did not report any parental actions encouraging Korean language use and cultural connection. This was contrary to my hypothesis, which predicted that greater parental willingness will correlate to greater willingness among adolescents. This may suggest that Korean-American adolescents may be more motivated by intrinsic factors instead of extrinsic incentives. Furthermore, parents who attempt to encourage their children to maintain the Korean language and culture may risk harming their children's natural motivations, per the overjustification effect, which states that "extrinsic rewards undermine intrinsic motivation" (Levy et al.). Hence, it can be advised that parents should avoid taking any action to influence their children's attitudes toward heritage retention.

Attendance of or affiliation with a Korean church also showed no noteworthy correlation with levels of willingness. Many participants expressed a desire to retain the Korean language and culture regardless of whether or not they were affiliated with a Korean church. In fact, 100% of those who were not affiliated with a church expressed very positive attitudes (Likert value of 5) towards language and culture maintenance, whereas less than half of those who were affiliated with a church expressed very positive attitudes. Though this data may imply that no affiliation with a church has a positive correlation with levels of willingness, the sample size of those with no affiliation (p=4) is not large enough to solidify that conclusion. However, it can be assumed that though Korean churches serve as rich ethnic and cultural centers, they are not the only way to immerse oneself in one's heritage background, and certainly not the most dominant. Korean-American adolescents can still find ways to explore their heritage language and culture without attending church, such as watching Korean variety shows, cooking and eating Korean food, and celebrating traditional holidays with their families.

Furthermore, the number of Korean friends was not a significant indicator of participants' levels of willingness to maintain their heritage language and culture as there was no clear pattern that suggested any correlation.

The qualitative data identified general reasons that may contribute to the adolescents' preferences of whether or not to maintain. Analysis of open-ended questions led to the interpretation that Korean-American adolescents make their own decision to maintain the Korean culture or language. Korean-American adolescents in southeastern Michigan overall expressed a desire to continue their practice of the Korean language and preserve their connections to the culture, supporting my hypothesis. This may be due to the fact that southeastern Michigan has many traces of Korean culture, from restaurants and churches to K-pop stores and Korean grocery stores. Furthermore, the sentiments expressed suggest that assimilation is not significantly present among Korean-American adolescents in southeastern Michigan.

Conclusion

This study aimed to identify factors that correlate with varying levels of desire among Korean-American adolescents in southeastern Michigan to maintain their Korean language and culture. Per the results of the survey, the majority of respondents indicated that they were intrinsically motivated to continue practicing their Korean language and culture. However, the age of an adolescent was the only factor that identified a difference in the level of desire to do so: older adolescents tended to value maintaining their heritage language and culture more than younger adolescents. This suggests that assimilation into American culture is not a high concern among Korean adolescents and therefore indicates that there is very little need for concern regarding a loss of Korean language and culture among future generations. While previous studies were largely centered around the perspectives of Korean-American adolescents' parents, this study successfully closed the gap by gaining insight into the perspectives of the adolescents themselves. Certain limitations of this study should be considered in future works in order to improve on or add to the current understanding. Since there was a limited number of factors analyzed, additional studies should be expanded to consider more potential factors, such as the number of years residing in the U.S. or peer pressure to speak English. Due to the researcher bias mentioned earlier in the methodology section, the analysis of the open-ended questions may have been influenced to reflect the researcher's opinions. Therefore, open-ended questions should be analyzed and categorized by a person of an objective and neutral background in future studies. In addition, a lack of knowledge about each respondent's unique experiences and background made it difficult to accurately predict and anticipate potential factors..

This study holds significant implications for future direction. It demonstrates that any parental action is not necessary for motivating children to maintain their Korean language proficiency and cultural connection. In addition, Korean organizations should gear outreach efforts toward a younger audience in order to encourage and maintain adolescents' desire to retain their cultural heritage. Through actions such as this, Korean-American adolescents can be inspired to find pride, excitement, and interest in their heritage language and culture, and Korean culture in the U.S. can continue to thrive and grow.

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Exposing Video Games By Lucas Lim

Abstract: Many studies have shown a connection between violent video games and an increase in aggressive behavior and attention deficit symptoms, as well as a decrease in prosocial behavior and academic success. However, when adjusting for faults in methodology, the connection is much less defined. In fact, many studies have shown an increase in certain cognitive functions and ability to learn new tasks after playing action games. Not only can commercial video games improve cognition, but educational games have also been shown to aid in learning. Overall, the common belief that violent video games can cause violence is not well supported by previous studies, while evidence in support of positive cognitive effects is growing.

For years, many have believed that children playing video games suffer from myriad negative effects, including but not limited to increased aggression and decreased academic performance. However, this point of view has recently been called into question by researchers[1,2]. Because of both research into positive effects of video games showing significant increases in cognition and ability to learn new tasks and prior studies showing negative effects coming under scrutiny, we have reason to believe that video games cause more good than harm.

Many researchers have reported a link between violent video games and negative outcomes regarding mental or behavioral health. In fact, taken in aggregate, 101 studies show a slight decrease in prosocial behavior and an increase in attention deficit symptoms and aggression[2]. In addition, several professional organizations like the American Psychological Association and the American Academy of Pediatrics have, to differing degrees, supported the position that video games can increase aggression[2].

Many researchers used the Taylor Competitive Reaction Time Test (TCRTT) to measure aggression. In this test, a participant attempts to push a button faster than their opponent. If they fail they are subjected to a blast of noise, and if they succeed then they set an intensity and duration of a sound blast for their opponent, the louder and longer the blast the more aggressive the participant was deemed to be. One study found that players were more likely to subject an opponent to longer and louder blasts of noise after playing violent video games, and concluded that video games result in increased aggression[3].

However, these studies and tests suffer from flaws compromising their validity. First, the TCRTT is not solely a measure of aggression. Since participants are led to believe that a blast of noise may hinder their opponent's performance, the increase found by researchers like Anderson and Dill using the TCRTT may not be in aggression, but rather competitiveness.

In addition, the games compared in many studies differ not only in violence but in other factors which muddle their results. For example the experimental group may be playing a video game that is more violent than the control group, but that game may also be faster paced, more difficult, and more competitive[1,2]. With so many variables changing between the control and experimental group, it's difficult to attribute any effects to the violence of the video games.

Many studies also failed both to pretest participants and to provide a suitable control group[1,2]. Because of this, it is easy for researchers to misinterpret results. For example, since we

don't know how aggressive participants were before they played a given game, a study which claims to show increased aggression in participants who played violent video games may actually show no change in aggression in them, but rather a decrease in aggression in those who played non-violent video games, or even a decrease in aggression of both, but the latter at a faster rate. This ambiguity calls into question the validity of the results of these studies.

Moreover, a significant number of studies have neglected to consider the effects of third variables. Once third variables like gender and mental health are accounted for, the slight decrease in prosocial behavior and academic performance and increase in attention deficit symptoms, depressive symptoms, and aggression almost entirely disappear[2]. One possible reason that this problem plagues so many studies in this field is that many researchers are prone to selective interpretation, and may report bivariate results but not more accurate multivariate results if the bivariate results support their hypothesis and the multivariate results do not[2].

An example of the significance of third variables comes from the issue of correlation versus causation. Correlational studies reporting that players of violent video games had increased aggression, attention deficit symptoms, etc., may be looking at data that shows violent video games are correlated with those symptoms but do not necessarily imply causation, and could instead be the result of a third variable. For example, an adolescent with a dysfunctional family may suffer from increased aggression as a result of repeated exposure to stressors in their life. They may also seek out video games as a means of escape. In this scenario a dysfunctional home life caused both video game play and aggression, and their statistical correlation is due to the confounding variable. However, a researcher conducting a correlational study would simply see a person who is both more aggressive and plays violent video games and may assume the causation that fits with their hypothesis.

In addition to calling into question the negative effects of video games, recent research has also demonstrated benefits to cognitive performance for video game players[4,5,6]. One study investigating a possible method by which video games can improve performance in a variety of cognitive abilities randomly assigned participants to play action video games or simulation games for 45 hours[6]. They found that participants randomly assigned to play action video games, similar to the ones maligned by prior researchers, actually had an increased rate of improvement in novel tasks across cognitive domains, or an improvement in ability to learn, relative to participants who played simulation games.

Another study showed similar results, indicating that commercial video games may have potential to increase visual attention and rapid visual information processing[5]. The researchers performed a correlational study, comparing video game players to non video game players. Those who played video games frequently had a greater attentional capacity than those who did not. However, this study is not perfect since it only demonstrates correlation and not causation. While a possible takeaway of this study is that playing video games increases your attentional capacity, an equally plausible alternative is that people with higher attentional capacities are better at video games and are therefore more likely to play them. To combat this, the researchers also performed an intervention study on some of the non video game players. The control group

was trained on Tetris, a puzzle game, and the experimental group was trained on Medal of Honor, a first-person shooter action game. Each group trained for 10 hours, and then were tested on their visual attention skills. In all three tests the experimental group outperformed the control, which the researchers believed was because experimental participants had to split their attention to a much greater degree, while in the control a participant must focus on one object at a time.

Not only do commercial video games positively impact people, so too do educational games designed to aid in learning. Researchers have theorized that games make for an ideal learning environment because well designed games meet many criteria for experiences to translate to learning[7]. For example, the criteria for transfer of learned information, or "good learning," are that the experiences are designed with goals in mind, they are interpreted, players receive feedback, they apply what they've learned to new situations, and they interpret and explain their experiences with peers. Gee theorized that since these criteria are also important for video game design, well designed games have high potential for aiding learning in the classroom. Gee also stressed the importance of the social aspect of learning, arguing that the social settings surrounding games encourage reflection and interpretation, which are vital for learning transfer. He also emphasizes the importance of the "subtle" way in which games teach content, as opposed to traditional instruction's more "direct" approach[7]. The former is a much more active approach to learning than the latter, since it encourages students to actively participate in their own knowledge construction, thus retaining information much better. Through the lens of modern learning theory, because of the relative agency of students playing games, we would expect to see better results from them than from those engaging in more traditional forms of education[8].

This hypothesis has been supported by many experimental studies as well. In a study on comparing traditional to game based learning, researchers found that students using an augmented reality game to learn about medieval Amsterdam scored significantly higher on tests asking them to recall factual information than students who took traditional classes[9]. Another study had an experimental group of students playing an online game with web based problem solving activities and a control group of students using traditional paper worksheets. There were a total of 50 participants in 5th and 6th grade split into the two groups. The experimental group played a game in which they rolled dice, moved around a board, and completed a gaming task corresponding to the space they landed on. These tasks included multiple choice questions, web based problem solving, and mini games. The control used traditional learning sheets. The experimental group had significantly higher learning achievement, learning attitude, flow experience, and learning interest[10].

To be most effective, people creating educational games must keep in mind preexisting cognitive science principles and use what we already know about how people learn to optimize transfer. For example, a study on embedded learning supports in educational games found a significant increase in far transfer of physics knowledge in students who played a version of the game Physics Playground with embedded learning supports compared to those without them[11]. In

this way, not only can learning science inform video game research, but vice versa as well. Video games may present a new frontier to explore the question of how we learn.

To summarize, while many believe that video games, specifically violent action ones, can cause increased aggression in players, the evidence behind this viewpoint is shaky, and in fact these same games can increase performance in several cognitive fields. In addition, games have tremendous potential for aiding learning in the classroom, and with learning supports that are being developed right now, this potential is only increasing. With support from you, the reader, we can shift the social perception of video games from the misinformed viewpoint of yesterday, to the more accurate, more optimistic viewpoint of tomorrow, in which video games not only have a measurable impact on people's attentional and cognitive abilities, but also have an immense potential to shape both the education of students and the learning and skill training of people everywhere.

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Explore/Exploit Tradeoffs in Human Decision Making: A Brief Review By Krish Bahel

Abstract

Explore-exploit tradeoffs–the conflict between *exploring* novel options and *exploiting* familiar ones–is a fundamental decision model adapted from basic and translational science. Striking the right balance between these two strategies is pivotal for achieving efficient outcomes and adapting to varying levels of uncertainty. Individuals must also adapt to varying levels of confidence and external factors that hold implications for their decisions. This review aims to shed light on the influential role of various cognitive (e.g., confidence, bias) and affective processes (e.g., stress) on explore-exploit decision making. We also cover the role modern neuroscience has played in studying this tradeoff and its underlying neural circuitry. This topic holds profound importance in making real-world developments across diverse disciplines. In economics, understanding how confidence impacts decision making can elucidate market behaviors and financial choices. In addition, this research advances models of artificial intelligence and human-computer interaction (HCI), which are highly reliant on understanding principles of decision. Lastly, understanding the underlying brain pathways can provide psychological insights into cognitive flexibility, motivational tendencies, and human learning; indeed, these are critical processes that, if perturbed, underscore the etiology and maintenance of a variety of psychiatric illnesses.

Keywords

Behavior and Social Sciences, Cognitive Psychology, Decision Making, Explore-Exploit

Introduction

Dining at your usual spot for burgers or venturing to the new dumpling restaurant down the street is a mundane decision with relatively low stakes. However, at its core, this reflects a conflict between explore and exploit motivations. The conflict splits the highway of our neural decisions into two separately winding roads: Do you want to continue *exploiting* the great taste that you know and love, or do you want to *explore* alternative options and maybe find a new favorite? This dynamic interplay is a theme that courses through our lives, underlying many human behaviors and prompting us to contemplate whether to tread our familiar paths or venture into uncharted territories of inquiry. Interestingly, clinical research suggests studying explore-exploit decision making in humans may help improve our understanding of transdiagnostic features of various psychopathologies (Addicott et al., Letkiewiczet al., Linson et al.).

From research in economics to neuroscience, explore-exploit decision making has been extensively explored; indeed, recent work has begun to pursue a mechanistic understanding of these computations (Addicott et al.). This work not only deepens our comprehension of cognitive processes governing our choices but also broadly contributes to an evolutionary brain-behavior

framework for understanding how we traverse the complexity of our environment. In this brief review, we first go over common approaches and paradigms that cognitive neuroscience has used to advance our mechanistic understanding of explore-exploit decision making in humans. Second, we cover the neural underpinnings of the explore-exploit dilemma in addition to cognitive and emotional aspects. Lastly, we will discuss clinical relevance and real-world implications of this research.

Results and Discussion-*Assessing exploration and exploitation in humans*

Neuroscience has advanced our measurement of explore-exploit tradeoffs in exciting ways, adapting human-appropriate paradigms from basic and translational science and leveraging multimodal neuroimaging, eye-tracking, real-time psychophysiology, and other cutting-edge technologies (Roselli et al.). These methods help achieve a deeper mechanistic understanding of this phenomenon. By utilizing these paradigms and neuroimaging technologies, scientists can design experiments and studies that offer valuable insights.

Slot machine tasks and multi-armed bandit paradigms have been go-to experimental paradigms for studying exploration and exploitation in humans. These bandit and slot paradigms primarily rely on the gambling instincts of participants to reflect individual- or group-level patterns of resolving competing motivations. To foster authenticity, tasks often incorporate real monetary-based conflicts and other impacts to probe "real" decision conflicts in digital environments (Raja Beharelle et al.). To this end, many of these slot machine and multi-armed bandit tasks are completed on a screen or even online. Participants must decide whether to persist in *exploiting* rewards offered by their current machine or to cast their gaze outward, *exploring* novel options in the pursuit of more favorable outcomes. In slot machine paradigms, participants gamble as if they were genuinely playing at a set of regular slot machines, aiming for the highest payout (Boldt et al.). Many papers define the act of switching machines as *exploration* and the act of continuing at the same machine *exploitation* (Blanchard & Gershman, Laureiro-Martínez et al.). Multi-armed bandit tasks are a bit more complex; here, there are multiple slots that have different reward outcomes. Participants also are typically asked to complete subjective ratings after each trial, measuring contributions of emotion and confidence in decision-making (Boldt et al.).

These paradigms also have their drawbacks. First, there has long been concern about how lab-based paradigms translate in real-world contexts. For instance, people may be more likely to exhibit more explorative tendencies when in the lab which could reflect how participants are appraising stakes. Additionally, we may lose important ecological context by oversimplifying decision conflicts in lab environments that become learned after numerous trials (Kashdan & McKnight). Other paradigms do exist, however, they may be better suited for other types of decision conflicts such as go/no-go for approach-avoidance conflicts (Bari & Robbins). Indeed, we are due for major advancements in mechanism-focused explore-exploit tradeoff experiments that prioritize ecological validity while preserving rigor and ethics.

As these paradigms and experimental designs facilitate the accumulation of data, various tools of neuroscience are poised to quantify brain activity during explore-exploit decision making. Functional magnetic resonance imaging (fMRI) and electroencephalogram (EEG) have been two widely used neuroscience tools for acquiring brain data while participants perform tasks. While both are useful for detecting brain activity, EEG specifically records electrical responses and is known to have better temporal resolution (i.e., real-time data acquisition). In contrast, fMRI records hemodynamic responses and yields better spatial resolution. Both EEG and fMRI are critical to identifying neural correlates associated with exploration and exploitation strategies (Nunez & Srinivasan).

Effectiveness has been found with usage in the animal literature and translation over to humans. For example, in studies involving chimpanzees, EEG has been used to uncover the biology of value setting in primates. Findings from Averbeck and Costa show how setting expected values for specific circumstances involves various regions of the brain, including the orbitofrontal cortex and ventral striatum, which are responsible for emotion and reward processing. These Initial and Final Expected Values (IEV and FEV, respectively) are correlated with how an individual would choose between taking an explorative pathway rather than an exploitative one. A high IEV would suggest significant rewards, potentially influencing exploitation. A low IEV, however, would suggest low or uncertain rewards and may influence exploration. FEVs represent values obtained by participants. High FEVs may incentivize repetitive exploitation. On the other hand, fMRI captures changes in blood flow and oxygenation levels in various brain regions, commonly known as BOLD, or Blood Oxygenation Level Dependent (Logothetis & Wandall). By studying morphometry and activation of different brain areas, researchers can identify regions associated with exploration, exploitation, and the dynamic interplay between the two. Since decision encompasses complex cognitive processes that likely are supported by distributed neural activity, many researchers use BOLD activation to provide insight into connectivity across different regions. In short, connectivity between regions is inferred when two or more brain regions show similar activity while performing an action (Poldrack et al.) . Assessing the physical structure of the human brain is just one of the fMRI's many important applications. By studying structural differences between individuals, researchers can detect variations in different regions and how they could create individual cognitive differences (Lauriero-Martinez et al.). In the context of Human-Computer Interaction (HCI), researchers' methodology aligns with the objective of understanding how users navigate digital interfaces during exploration and exploitation tasks. By leveraging established HCI paradigms, they aimed to uncover user behaviors and decision-making patterns within real-world digital environments. For example, many of these slot machine and bandit paradigms can be completed on a screen or even online.

The neuroscience of explore-exploit decision-making

Researchers have made significant progress in understanding the biological foundations of explore-exploit tradeoffs. They have identified particular brain areas that are more active

throughout each of these decision-making pathways with fMRI. Blanchard and Gershman noted the ventromedial area of the prefrontal cortex (PFC) is significantly more active during exploitative actions. In their study, Lauriero-Martinez and colleagues, the ventromedial PFC consistently emerged as an active region during exploitative tasks, reaffirming its role in encoding Immediate Expected Value (Lauriero-Martinez et al.).In contrast, when exploring more novel decision-making territory, Daw & colleagues found the frontopolar cortex (FPC) to be relevant. A recurrent theme in these papers and articles is the definition of exploration, often defined as a participant departing from their current course of action, akin to switching from one slot machine to another. Building on these insights, Lauriero-Martinez and her colleagues reported heightened FPC activation during explorative activities. Notably, their findings also revealed activation in other regions associated with attention control, such as the temporoparietal junction and the superior parietal lobule, indicating potential functional connectivity among these brain regions. These collective findings suggest a network of interconnected regions that collaborate in decision-making processes.

Cognitive factors

Extant work has focused on identifying key cognitive processes relevant to resolving explore-exploit conflicts. One fundamental cognitive process at play is our capacity for risk assessment. When faced with the choice of venturing into the unknown or sticking with familiar territory, our brain engages in a sophisticated evaluation of potential risks and rewards. This cognitive weighing of uncertainty versus predictability impacts whether we lean towards exploration or exploitation. Dombrovski and Hallquist highlight how variations in cognitive risk assessment may be associated with addictive tendencies, underscoring the intricate link between cognition and behavior. In addition, delay discounting, favoring (smaller) immediate over (larger) delayed rewards, seems to influence explore-exploit decision making significantly. Those with higher delay discounting tendencies prioritize immediate gains (exploitation), while those with weaker tendencies prefer assured but delayed rewards (exploration), compromising long-term decision-making (Dombrovski & Hallquist).

Further, memory and immediate processing seem to be influential to our decision-making calculus. When considering exploration, our brain draws upon past experiences stored in long-term memory to assess potential outcomes, while short-term memory aids in processing the immediate information available. In turn, this adds personal biases and learning into the equation. Blanchard and Gershman show how people are more likely to be exploitative after learning patterns or tendencies. For example, if an individual realizes that a game of online poker is patterned to have twice as many rewards in every third round, they are more likely to bet more on the third round to exploit higher rewards. In their study, participants are asked to bet on the color of the light, which has been patterned, that they expect to flash in front of them. After learning the pattern of light colors, they switched to more exploitative decisions and betted more frequently. Lastly, confidence also has been shown to play a role in explore-exploit decision making. According to Boldt & colleagues, participants with a higher confidence rating report

being more sure of their exploitative behaviors. They are more likely to take risks involved with deciding to remain with their current bandit, exhibiting higher exploitative tendencies.

The role of emotion

Since the rise of affectivism, inclusion of emotion and affect on behavior, there has been an influx of research focusing on the role of emotions in decision making. Emotions appear to hold a strong basis on whether a person is explorative or exploitative. For example, stress can produce a strong desire for avoidance and a distaste for exploration. Under stress, people may choose to exploit their current source of reward due to the risk of exploration (Aberg et al.). While weighing their options, people may feel that trying new things leaves them vulnerable to mistakes, harsh judgment, or even danger. However, emotions also motivate exploratory behaviors in some cases. Findings from Kashdan and McKnight suggest that happier moods are connected with explorative tendencies. Those with intrinsic interests and joy from a topic can directly contribute to a pattern of exploration in that field. This relationship between happiness and exploration is profound, as it not only initiates the journey into the unknown but also sustains it over time. When individuals find genuine delight and fulfillment in their exploratory pursuits, positive emotional reinforcement encourages them to delve deeper into their chosen paths of discovery. Once again, the interplay between behavioral and cognitive elements may be crucially moderated by affect, creating a synergy that collectively shapes our decision-making.

Clinical Implications

The clinical impact of explore-exploit research promises to be extensive. For instance, work from Dombrovski and Hallquist suggests increasing our understanding of the tradeoff between these behaviors could help lower suicide rates. A better understanding of how people experiencing suicidal ideation prepare themselves and their internal thought processes may initiate the development of better treatment plans or prevention programs. Additionally, research in this field has significant implications for the treatment of addictions and impulsivity. Bechara suggests individuals struggling with addictions display higher impulsivity and lack of patience or control. In this work, Bechara delves into the neural mechanisms underlying impulsive behavior, shedding light on cognitive processes (e.g., executive functioning) that contribute to exploitative tendencies in addicted individuals. By emphasizing the role of impaired executive function and willpower, Bechara's work highlights how addiction can disrupt the balance between exploration and exploitation in decision making. If able to disrupt this pathway of excessive exploitation to addiction, researchers will be able to provide a significant impact on the addiction world, whether it is gambling, substance abuse, or other forms of addiction. In conclusion, if researchers can continue uncovering the intricacies of explore-exploit decision making, they can continue paving the way for stronger clinical treatments and resources for complex conditions.

Future Directions

An integrative approach to studying explore-exploit decision making has been integral to advancing our mechanistic understanding of explore-exploit decision-making, although significant bounds are yet to be made. Even with new technology and methods, many findings are correlational, and little work has attempted to delineate causal relationships between brain processes and explore decisions in humans. In one of a few examples, Raja Beharelle and colleagues suggest that administering anodal transcranial DCT to the frontopolar cortex led to slower, exploratory-type decisions. Further, a cathodal transcranial DCT led to quicker, exploitative-type decisions; indeed, these findings are not well replicated. Nonetheless, more studies looking to draw causal conclusions will undoubtedly fill a major gap in the current literature. Trials like these, ones that manipulate biological variables, are rarely seen far and wide for a reason. To manipulate any biological aspect, the possible benefit of this change must significantly outweigh the risk that the participants are undertaking.

As we continue to advance how we assess explore-exploit pathways, more real-life impact opportunities will appear. For example, the technological advancement that has accompanied this research is especially exciting. With advancements in the field, countless different technological products could be considerably improved. For example, artificial intelligence and machine learning models will be able to quantify human data at a significantly higher rate, understanding their consumers better and improving efficiency. Further, in the realm of content recommendation algorithms, a better understanding of explore-exploit dynamics may yield more personalized and engaging recommendations for users, boosting user satisfaction and platform engagement, while also potentially revolutionizing the way we consume and interact with digital content. In economic decisions, these insights could lead to more efficient resource allocation and investment strategies, ultimately enhancing economic growth and bolstering financial stability.

Conclusion

The current review briefly examines the complex dynamics underlying exploration and exploitation decisions. Paradigms informed by translational science have been useful for testing explore-exploit tendencies in humans, however, we should consider improving these paradigms to increase ecological validity. Advanced methods from psychology and neuroscience have spearheaded the movement toward a mechanistic understanding of exploration and exploitation, with a particular focus on the ventromedial prefrontal cortex (vmPFC) during exploitative behaviors and the frontopolar cortex during more exploratory decisions. Exploring the cognitive and emotional aspects of explore-exploit decision-making has also shown the influence of factors like risk assessment, memory, and emotions on our choices. We now have a mechanistic understanding of how these processes affect people's decision-making as a result of this lengthy examination. Our field has surpassed a mere theoretical perspective of explore-exploit decision-making; advances will improve operations across several disciplines, including economics, artificial intelligence, and clinical psychology.

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To What Extent Do Non-State Actors Impact Societies In Developing Countries? -Taking an Example of NGO In Nigeria By Jinyang Dong

Introduction

Non-State actors are becoming increasingly active in the international arena. The globalization and the information technology diffusion has enabled more rapid information access and dissemination, as well as cross-border organization and collaboration for non-State actors[4]. The limited resources of the State provide opportunities for cooperation between state and non-State actors. In fact, some multinational organizations are influencing government policies and decisions through public opinion and cooperation[5]. On the other hand, most developing countries are facing economic, social, and environmental challenges, requiring scientific, technological, and developmental solutions. This has allowed non-state interactions in such nations, the scale and potential of which has expanded significantly. One of the most noteworthy aspects of this is the interaction between NGOs and developing countries[6].

In general, NGOs are mostly non-profit organizations, although they include for-profit organizations as well. NGOs' focus on broader social and global issues positions them to meaningfully engage developing countries. In this regard, this paper examines the impact of non-state actors on societies in developing countries.

Case study of NGOs in Nigeria

As the birthplace of influential early civilizations, Africa is now home to the largest number of developing countries in the world. Most of them score relatively low on development levels, with some regions among the least advanced globally. Africa's large population and resource wealth coexist with acute conflicts, human rights issues, and social challenges. As the African country with the largest population, Nigeria is at the same time a multi-racial and multicultural country. It is also one of the largest oil producers in Africa, and with it comes many economic and environmental problems. Nigeria has experienced a number of regional and religious conflicts, which have brought great instability to the development of the local society. Nigeria, as a huge sample, has given NGOs enough ground to make a difference.

Although the Nigerian government has responded to these insecurity, economics and environmental problems to some extent, it has not significantly improved the problem due to its own financial and capacity constraints. In recent years, as the number of NGOs has increased, more and more NGOs have begun to pay attention to Nigeria's development issues and are committed to helping Africa's largest developing country tide over its difficulties. Through ongoing efforts, NGOs have achieved positive regional results, complementing government efforts via utilizing management, technology, and information capabilities. Thus, this paper

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reviews the problems that Nigeria faced in the last few decades, and then examines the actions of NGOs in Nigeria.

Insecurity

First and foremost is Nigeria's security problem. Boko Haram is one of the most rampant terrorist groups in Nigeria. It is an Islamic ultra-fundamentalist organization with its main activities in northern Nigeria. Boko Haram's aim is to oppose Western culture and education, and to promote Western education as a sin that blasphemes Islam. They advocate for the imposition of strict Sharia law in the northern states of Nigeria. Known as the "Taliban of Nigeria"[7], Boko Haram opposes Western culture, modern science, the Western education system, votes in democratic elections, shirts and shorts. Their activities include attacks on government forces, abduction of civilians and students, destruction of schools and infrastructure, etc. These terrorist activities have led to a large number of casualties, family breakdowns and humanitarian crises.

Religious demographics in Nigeria split roughly equally between Christianity and Islam, concentrated in the south and north respectively. Most of the Christians here are sedentary farmers, while the Muslims are mostly nomads. For more than half a century, due to the intensification of climate change and the prolonged droughts, many areas in northern Nepal have desertification, forcing herders to move southward, some herders choose to graze permanently in the central belt, and temporary hospitals and schools have been built, triggering disputes with local farmers over land and water use rights[8]. These conflicts often turn into bloodshed, creating instability in production and internal hatred.

In addition, Nigeria faces threats from criminal activities including robbery, drug trafficking, human trafficking, and kidnapping[9]. These crimes not only seriously affect domestic security and social stability, but also cause problems for foreign investors and undermine local development opportunities.

Such widespread insecurity spurred diverse NGO involvement in conflict mitigation efforts. Although there are no armed forces, NGOs still provide assistance in Nigeria when facing security issues. Boko Haram has always been a major threat to Nigeria's security and stability. The government has repeatedly urged the military to carry out crackdowns, but the danger of Boko Haram remains serious.

The NGO Conciliation Resources(CR) promotes conflict resolution through inclusive dialogue". Please also feel free to make changes. Years of work experience have made the CR realize that communities in northern Nigeria are extremely unstable. This has led to the young people detached from civic structures for many years, and a considerable number of people have joined the terrorist organization Boko Haram under coercion and inducement.

To address this situation, the CR mobilized young people from northern Nigeria. The organization provides training, guidance, and support to young people, not only restoring their

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confidence from the turmoil and dealing with their past traumas, but also calling on them to join in peacebuilding[10]. With the efforts of the organization, over 3000 young people have received assistance and joined the cause of peace building. The conflicts in multiple communities have been alleviated, and the lives of ordinary people are on track. "Whether we like it or not, youth have been at the center of the violence, it is our brothers and sisters who were part of this group, who have been killed, abducted, arrested or whatever. That is undeniable. But what I see now is that the youth also have the potential to end the violence and bring peace to communities." said Idris Abdullahi, Youth Peace Platform chairperson from Damaturu, Yobe State[11].

In fact, NGOs are well-positioned to facilitate conflict resolution due to their impartial nature and emphasis on humanitarian objectives. Members within NGOs often have professional skills and negotiation skills, coupled with humanitarian assistance, to establish good connections with the public. Therefore, promoting conflict reconciliation through dialogue among NGOs is the most recognized and recognized way to resolve conflicts. Conciliation Resources also organized dialogues between conflicting tribes in Nigeria, as well as between various religions and ethnic groups. Many NGOs are also alleviating violent conflicts by promoting communication and mutual understanding. This has made critical contributions to peace and social stability in Nigeria.

Besides dialogue-promoting, Conciliation Resources creates a peaceful and stable social environment by helping the youth. Engaging more young people is also an effective way to address conflict issues. The Catch Them Young Initiative is a leadership training program initiated by CPPBI(Conflict Prevention and Peace Building Initiative) for young people. They have established different clubs in some schools in Nigeria and conducted a series of training and exchange activities. These activities not only impart peaceful thinking and conflict resolution skills to young people, but also help them find their own direction in life in a turbulent society. These schools have effectively addressed the educational needs and challenges faced by underprivileged youth, gaining recognition from multiple universities and colleges in Nigeria, such as Benson Idahosa University and Wellspring University, Bishop Gordon Educational Academy[12]. Having youth engagement stimulates their vigor and benefits the society through their help, which is conducive to long-term development.

In general, NGOs have greatly contributed to resolve the insecurities in Nigeria. Their works are effective in some regions, not only deterring conflicts, but also showcasing a potential for long-term development. Nevertheless, their scale still needs to disperse in a wide range of regions. The observed rise in atrocities and deaths, as documented in the Nigeria Mourns' Mass Atrocities Report[13], could potentially be attributed to the epidemic situation. However, this upward trend underscores the challenges that remain in addressing Nigeria's security issues.

Economic Problems

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[10] https://www.c-r.org/our-work-in-action/young-people-prevent-violence-northeast-nigeria

[11] idem
[12] https://www.peaceinsight.org/en/organisations/cppbi/?location=nigeria&theme
[13] https://www.nigeriamourns.org/media-reports/?_page=2

Despite being the largest economy in Africa, Nigeria still faces serious economic problems. Nigeria has huge oil and gas reserves, but it lacks extraction and refining technology, and needs to cooperate with foreign companies. Thus, while oil has generated huge economic benefits to Nigeria, a significant portion of the proceeds have been distributed to foreign technology companies. Oil exports are the main source of national revenue for Nigeria. Therefore, Nigeria's economy is heavily dependent on oil. Nigeria's economic development is very precarious due to its relatively homogeneous economic structure[14].

A considerable number of people live in poverty, and in order to scrape a living, they begin to steal oil in groups and sell it in local black markets. The massive oil theft has had a huge negative impact on Nigeria's oil and gas sector[15]. According to The Nigeria Extractive Industries Transparency Initiative (NEITI), Nigeria has recorded 7,143 cases of pipeline breakages and intentional vandalism, which consequently led to 208,639 million barrels of crude oil being stolen. The faulty petroleum devices may cause massive environmental pollution. In the face of rampant oil theft, the Nigerian authorities seem powerless. As a result, the market was flooded with low-quality gasoline, and many oil companies had to withdraw by "tapering down investment and shutting down wells" – oil production falls significantly below the OPEC target of 1.8 million barrels per day[16].

Nigeria's unemployment rate has remained perennially high, accompanied by the highest number of annual births in Africa each year, and its total population is expected to surpass China's by 2100. The combination of a poor economy and an extremely high unemployment rate has forced most Nigerians to endure poverty and hunger. The gap between rich and poor is widening, and a few people enjoy more resources and opportunities[17]. The uneven distribution of infrastructure and public services further increases the risk of social unrest and crime.

Poverty constitutes a significant societal challenge, leading to increased crime rates and widespread hunger. To create job employment, many NGOs and firms collaborate together. A case study by Ejiro U. Osiobe shows the economic impact of Non-Governmental Direct Investment from NGO[18]. It infers that investment to the local community can be very beneficial to job creation and income increase. So, NGOs are encouraged to expand their investment in local societies. Another study also supports this argument and advocate for the involvement of NGOs in rural areas and invest on health care, education and industries[19].

Leadership Initiatives(LI) launched by Global Giving aims to foster entrepreneurs from the

[14] Olomola P A. Oil price shock and aggregate economic activity in Nigeria[J]. African Economic and Business Review, 2006, 4(2): 48-61.
[15] Adishi E, Hunga M O. Oil Theft, Illegal Bunkering and Pipeline Vandalism: It's Impact on Nigeria Economy, 2015–2016[J]. International Journal of Economics and Business Management, 2017, 3(2): 47-65.

[16] Ayadi O F. Oil price fluctuations and the Nigerian economy[J]. OPEC review, 2005, 29(3): 199-217.

[17] Anyanwu J C. Marital status, household size and poverty in Nigeria: evidence from the 2009/2010 survey data[J]. African Development Review, 2014, 26(1): 118-137.
[18] Osiobe E U. The Economic Impact of Local Non-Governmental Direct Investment (s) on the Nigerian Economy: The Case of Lugbe, FCT, Nigeria[J]. The Ane Osiobe Trendsetters Series, 2019: 1-11.

[19] Agba A M, Akpanudoedehe J J, Ocheni S. Financing poverty reduction programmes in rural areas of Nigeria: The role of non-governmental organisations (NGOs)[J]. International Journal of Democratic and Development Studies (IJDDS), 2014, 2(1): 1-16.

people who suffered from unreliable infrastructure and a lack of economic development that have caused poverty and unemployment. By using the local resources, the LI hopes to tackle the issue through promoting connections and solutions within the community. The LI promotes grassroots social entrepreneurship to drive sustainable development. Compared to the other firms, local enterprises usually have a better understanding of the local social and market conditions. As well as familiarity with the preferences and habits of the local population. These advantages make the local enterprises more resilient and can also create more job employment and economic benefits. But still, there is a lack of funds and support to the organization and hence the LI didn't operate as expected.

Apart from leadership promotion, there are several NGOs that are providing necessary skill training and technical training for the local youth. Hope for Nigeria is implementing a Free Skill Acquisition Program for Nigerians. They aim to equip the youths with vocational skills that are necessary for entering the labor market. This includes water engineering and software production, website production and AI development, videography and cinematography, beauty production, fashion and textile production, art and crafts, and farming (agricultural or livestock). The training is totally free which gives opportunities for people living in poverty. As a result of the efforts of NGOs, the local workforce has become more productive compared to previous levels, leading to increased job opportunities, higher incomes, enhanced societal stability, and improved product and service quality. The provision of free training by NGOs has significantly alleviated financial burdens for individuals, thereby positively impacting their livelihoods.

On the other hand, the pollution problem caused by oil production has led to great concern. The environment of Niger Delta was severely polluted, and the communities living there, as well as the water resources have been contaminated. This has affected fishers and farmers, and created conflicts among people and oil companies. And the government refuse to regulate gas flaring, pipeline maintenance or levels of spillage, this increases the conflict and lead to violent clashes[20]. NGOs actively support the local people, exerting pressure on oil companies and filing lawsuits. With the continuous improvement of environmental protection laws in Nigeria, NGOs are capable to undertake increasingly effective measures to combat environment pollution[21]. However, there still need more NGOs to join and fight against oil pollution, oversee and encourage the public to report illegal pollution discharge and oil theft.

Education Challenges

The educational imbalance in between urban and rural areas deeply affects Nigeria. UNICEF's data highlights the alarming fact that Nigeria has the highest number of out-of-school children in the world, with at least 10.5 million children deprived of education. A full one-third of Nigerian children are not in school, and one in five out-of-school children in the world is

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[20] Ifeka C. Oil, NGOs & youths: Struggles for resource control in the Niger delta[J]. 2001.
[21] Anozie M C, Wingate E O. NGO standing in petroleum pollution litigation in Nigeria—Centre for Oil Pollution Watch v Nigerian National Petroleum Corporation[J]. The Journal of World Energy Law & Business, 2020, 13(5-6): 490-497.

Nigerian[22]. Overall, what Nigerian education needs most at the moment is funding. The government spending has been increasing since 2003, but is still unable to fill the huge gap of fund[23].

Urban areas have relatively better school facilities, teachers, and educational technology. While rural areas are facing a shortage of educational resources and limited enrollment opportunities. At the same time, Nigeria has many out-of-school children. Poor families cannot afford the school tuition fees. Moreover, factors such as conflict and terrorist activities can cause students to interrupt or even abandon their education. This phenomenon is particularly acute in the north.

Vulnerable populations consist of girls, children with disabilities, children from impoverished households, those in street situations, or affected by displacement or emergencies, and children in geographically distant areas are all dramatically affected by the education crisis. These vulnerable groups need special care and therefore more educational efforts and support are necessary and urgent.

Nigeria faces the problem of insufficient quality of teachers and education. Insufficient numbers of teachers, coupled with inadequate training and teaching skills, contribute to the quality of teaching[24]. Nigeria has a serious imbalance in the student- teacher ratio, and there has been a long-standing shortage of teachers. A large proportion of lecturers at universities are assistant professors without doctoral degrees: Reports from 2012 suggested that only 43 percent of Nigeria's teaching staff held Ph.D. degrees, and that Nigeria had one of the worst lecturer-to-student ratios in the world. The University of Abuja and Lagos State University, for example, reported lecturer to student ratios as high as 1:122 and 1:114 respectively[25].

At the same time, teachers' salaries are relatively low, which makes the teaching profession not attractive enough to recruit professional scholars, making it difficult to improve the quality of education[26]. Considerable cases of corruption such as paid-for certificate, 'special center' examinations, sexual indictment, extortion and leaked questions have been always emerged in schools[27]. This also includes cheating in exams, embezzlement by educational institutions and officials in the system. Serious problems of cheating and corruption in exams increased in the education system. This kind of dishonest behavior undermines the fairness and credibility of

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[22]
https://www.unicef.org/nigeria/press-releases/unicef-warns-nigerian-education-crisis-world-celebrates-international-day-education

[23]
https://www.premiumtimesng.com/news/top-news/218097-2017-budget-nigeria-fails-meet-un-benchmark-education.html?tztc=1

[24] Offiong A A, Akpan A G, Usoro S H. Funding of vocational and technical education in Nigeria in times of global economic recession[J]. AFRREV IJAH: An International Journal of Arts and Humanities, 2013, 2(2): 149-158.

[25] International Organization for Migration. 2014. Promoting Better Management, p. 21.

[26] Odigwe F N, Owan V J. Trend analysis of the Nigerian budgetary allocation to the education sector from 2009–2018 with Reference to UNESCO'S 26% Benchmark[J]. Odigwe, FN & Owan, VJ (2019). Trend analysis of Nigerian budgetary allocation to the education sector from, 2009, 2018: 1-14.

[27] https://dailytrust.com/quality-of-education-in-nigeria-we-need-to-do-more/

education, and deprives students of fair evaluation and opportunities.

Moreover, many students struggle to find jobs related to their majors after graduation, particularly in terms of skills training and practice. This has led to many graduates becoming unemployed or working in occupations unrelated to their majors, wasting skills and educational resources[28].

It is reassuring to note that in the face of numerous thorny problems, dozens of NGOs and foundations are committed to cope with the education crisis in Nigeria. Some NGOs raise funds and donate money to local schools. Notably, Siemens Stiftung, an independent nonprofit foundation established by Siemens AG in 2008, has partnered with the University of Lagos and invested to develop the Experimento project. This initiative focuses on enhancing STEM education (science, technology, engineering, mathematics) from primary school to university.

Furthermore, Donate-ng is a Fundraising and Donations Charity foundation that assists financially disadvantaged students by providing support for their tuition fees. It also facilitates entrepreneurial opportunities. They have helped students to raise an overall 192 million Naira, and thanks to their effective efforts on their platform and website, students averagely need about 4 weeks to hit their fund target. More and more NGOs notice and run sustainable programs to help the local students to be self-sufficient in financing their education.

Other NGOs focus on education for marginalized groups and people in remote areas. Population Media Center-Nigeria is consistently contributing to the PLANE Window 3, a part of the United Kingdom's Foreign, Commonwealth & Development Office (FCDO) funded "Partnership for Learning for All in Nigerian Education"[29]. They establish community-based groups to facilitate essential literacy education for out-of-school children aged 6 to 13. They also provide home based and remote learning for those children residing in insecure communities. The program has interventions and specific activities to support gender equality and children with disabilities to enroll and remain in education. Global Giving has also initiated several fundraising projects to help local out-of-school children by raising funds to build public schools in rural and remote areas. Their efforts have benefitted over 2000 children who live in rural areas and cannot afford tuition fees.

Global Partnership is holding in-service training to enhance the education quality in five Nigerian states: Kaduna, Kano, Katsina, Jigawa, and Sokoto[30]. The training included sufficient instruction in child-centered, gender-responsive teaching methods, and provided with specific techniques to improve student learning for example, reading techniques suitable for large class sizes. More than 130 thousand early grade teachers benefit from the training. They have also provided scholarships to 15,514 female teachers to upgrade and attain the National Certificate in Education (NCE). The Global Partnership has collaborated with the government sectors to improve the training of the teachers to strengthen their skill and ability and enhance the quality of school lessons.

The growing population continues to contribute to an increasing number of school-age

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[28] Akande T. Youth unemployment in Nigeria: A situation analysis[J]. Africa in Focus, the Brookings Institute, 2014.

[29] https://www.populationmedia.org/the-latest/nigerias-education-crisis-20-million-children-out-of-school

[30] https://www.globalpartnership.org/results/stories-of-change/nigeria-keeping-boys-and-girls-school-and-learning

children in Nigerian society, which means that the pressure of the education crisis is only getting worse. Although the special training provided by NGOs to local youth and children is very effective, it has not reached the expected number and scale overall. To address this, it is necessary to further expand cooperation with the government to promote the development and popularization of public education.

Health care and human rights

Nigeria's densely populated regions, perennial high temperatures and poor medical conditions make it a breeding ground for many fatal diseases. The number of hospitals and clinics in Nigeria is very limited, especially in rural areas. As a result, Nigerians often choose traditional healers or a complete absence of treatment when they get sick. Medical equipment in Nigerian hospitals is scarce, and most of the equipment has been in disrepair for many years[31]. Medical surveillance systems are ineffective and often error-prone[32]. Dependence on foreign imports for vital medicines and equipment makes these vital resources very expensive, burdening patients with substantial bills.

There is a shortage of professional nurses and doctors in Nigeria, and although there are some indigenous and traditional healers who can help in treating the disease, a significant number of patients are aggravated[33]. Nigerian citizens' insufficient public awareness regarding diseases and preventive measures hampers efforts to control disease transmission. Nigeria's healthcare system also lacks the capacity and systems to respond to diseases and emergencies. It also does not provide adequate protection and priority care for vulnerable groups such as infants, young children, the elderly, and pregnant women. Nigeria lacks an effective legal framework to support and protect the healthcare system, and lacks effective mechanisms to combat drugs and gambling.

A large number of NGOs and foundations are working to improve the health care condition in Nigeria. Among them, the APIN is committed to addressing public health issues in Nigeria through advocacy, innovation, and adoption of cutting-edge technologies. At the same time, they initiated large-scale testing for a variety of diseases in Nigeria, and the valuable data they collected helped to allocate and manage medical resources.

From October 2017 to September 2022, APIN has conducted HIV testing for a total of 6,237,049 individuals, including 911,815 children and adolescents aged 0-19 years. In total, 188,926 people tested positive for HIV, including 13,264 children and adolescents aged 0-19 years. As of September 2022, 388,163 people are being treated, including 23,346 children and adolescents aged 0-19 years. Most importantly, the viral load suppression reached 95%, corresponding to 334,678 individuals[34]. Besides, their other programs, such as Orphan & Vulnerable Program, have benefited millions of people and greatly improved the local health care

[31] Oyekale A S. Assessment of primary health care facilities' service readiness in Nigeria[J]. BMC health services research, 2017, 17(1): 1-12.

[32] Welcome M O. The Nigerian health care system: Need for integrating adequate medical intelligence and surveillance systems[J]. Journal of pharmacy & bioallied sciences, 2011, 3(4): 470.

[33] https://www.afro.who.int/countries/nigeria/topic/health-topics-nigeria
[34] https://apin.org.ng/wp-content/uploads/2023/07/IPIN-Icares-Key-Performance.pdf

condition.

Despite successes, according to the Final Performance Progress and Evaluation Report[35], there are still challenges in implementation because some of the measures are new that haven't been tested enough. APIN wanted to waive all fees for those helped, but the high cost forced them to charge. Consequently, they are actively seeking collaboration with the government to ease the financial burden on the people being helped. The APIN recognized the high rate of treatment interruptions and responded by adopting innovative approaches including smart technologies and patient surveys.

Nigeria's chaotic political antagonism and religious conflicts have led to mutual hatred among various forces. As a result, violent law enforcement and police abuses are commonplace. In addition, some gangs and tribes engage in criminal activities such as forced labor and human trafficking, especially child labor and sex slavery. Violent incidents frequently arise due to discrimination based on regional, religious, and gender differences, both between the North and the South and within various regions. Sexual violence, especially against underage female abuse and rape, is also particularly severe.

Nigeria has been experiencing various natural disasters and violent conflicts throughout the year, with a large population of areas without a fixed residence and losing their livelihoods. In order to address the basic needs of these populations in the face of disasters, other organizations such as Mercy Corps have helped build houses and provide water, food, and sanitation facilities in the northeastern region of Nigeria to help people overcome difficulties and save lives in times of emergency[36]. Médecins Sans Frontières (MSF) is a medical organization with tens of thousands of health professionals, logistics, and administrative personnel. They are committed to saving a large number of infants, young children, and pregnant women who are suffering from diseases and urgently need medical supplies and treatment in the turbulent situation in Nigeria. In 2022, they helped save hundreds of thousands of infants and children, receiving over one million patients[37]. Their intervention has contributed to the improvement of the medical conditions of people in several northern regions of Nigeria. In recent years, they have paid more attention to the malnutrition situation of local residents. The malnutrition situation of the people of Illya is mostly concentrated in the northeast and northwest, as it is often accompanied by various factors such as violent conflicts, hunger, climate change, and epidemics. MSF has established specialized outpatient therapeutic feeding centers and inpatient therapeutic feeding centers in these areas[38].

The provision of humanitarian assistance in Nigeria, despite its increasing scale, is constrained by the ongoing violent conflicts, epidemics, and natural disasters. These crises persist and continue to affect a growing number of individuals each year. Humanitarian assistance in Nigeria still requires strong support from the international community, and further mechanisms

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[35] https://apin.org.ng/wp-content/uploads/2023/07/Formatted_FINAL-PERFORMANCE-PROGRESS-AND-EVALUATION-REPORT-FOR-APIN-ICARES-PROJECT.pdf

[36] https://nigeria.mercycorps.org/what-we-do

[37] https://www.msf.org/international-activity-report-2022

[38] https://www.msf.org/neglected-malnutrition-crisis-threatens-thousands-children-northwest-nigeria

for responding to disasters and conflicts need to be established.

Government Failure

The Corruption Perceptions Index(CPI) is a tool of Transparency International(TI) for assessing the degree of corruption of countries globally. The full mark is 100 points, and the least is 0. The higher mark indicates that a country has less corruption and vice versa. According to the ranking, Nigeria scored 24 out of 100 points in the 2021 CPI and it's ranked at 154 out of 180 countries in the 2021 CPI, which has dropped five places compared to 149 in the 2020 CPI. Although the Nigerian government has claimed that they are working consistently to reduce corruption, but the ranking may be an indicator that corruption is getting worse in Nigeria.

In addition, electoral fraud in Nigeria has left the population dissatisfied with the government. Nigerian officials have resorted to bribery, intimidation and violence to gain power, which has further exacerbated public frustration with the government. Interestingly, in order to maintain their image and cope with censorship pressure domestically and internationally, senior Nigerian officials have deliberately cultivated and funded a number of pro-government NGOs[39]. These groups disguise themselves as civil society groups and glorify officials and attack their critics through the media, among other things. Through the control of public opinion, many illusions of development and progress have been formed in Nigerian society. This is not only a crime to deceive the population, but also a step backwards in the development of non-governmental organizations. These pro-government NGOs have not only exacerbated the failures of the Nigerian government, but have also contributed to the rigidity of the entire political system. This means that there is a lack of international and civil scrutiny of NGOs in Nigeria.

The failure of the Nigerian government has caused widespread discontent among the population. In response, some NGOs are working with civil society to strengthen oversight of political democracy and transparency in Nigeria. The Transition Monitoring Group (TMG) is the foremost independent civil society election observation organization, focusing on observing and monitoring political elections in Nigeria and promoting government accountability and feedback mechanisms to improve government transparency. In the civil society, they encourage and increase citizen political participation through advocacy, and widely promote democracy and human rights in education. They launched seminars, workshops, advocacy, and campaigns in a wide range, but there is still lack of validity and enforcement. Unless the Nigerian government is under intense pressure or determined to make a change, otherwise the corruption and remissness in Nigeria will hardly improve. According to DJ Smith, regardless of the independence of NGOs from the Nigerian government's control, as long as they have a positive democratic orientation in civil society[40], they can still contribute to advancing ideological awareness and raise the expectations of the Nigerian people.

Environmental protection and sustainable development

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[39] Page M T. Fake Civil Society: The Rise of Pro-Government NGOs in Nigeria[J]. Retrieved from Carnegie Endowment for International Peace website: https://carnegieendowment. org/2021/07/28/fake-civil-society-rise-of-pro-government-ngos-i n-nigeria-pub-85041, 2021.
[40] Smith D J. Corruption, NGOs, and development in Nigeria[J]. Third world quarterly, 2010, 31(2): 243-258.

Oil revenues are an important pillar of Nigeria's economy, but environmental pollution caused by inefficient oil extraction and technological backwardness is becoming increasingly prominent. Adjacent land, rivers and air are polluted, which seriously affects environmental safety and also poses a potential risk of disease. Nigeria is a water-scarce country, while the Christians in the south are sedentary farmers who have a high demand for water. The irrational water use practices of the government and factories and farms, as well as the pollution of water sources, have further exacerbated the water shortage in Nigeria. This poses an important challenge to the sanitation of the population. In order to develop the economy and exploit minerals, a large number of ecosystems such as forests and wetlands have been artificially destroyed. This not only reduces biodiversity, but also threatens ecosystem functions and people's livelihoods. Several natural disasters caused by climate change have dramatically increased the dangers to society in this land where ecosystems have been destroyed. In addition, the rudimentary waste and sewerage systems of urban life increase the risk of epidemic transmission in cities, and also pollute the land and water environment around cities.

There are multiple NGOs in Nigeria that promote environmental protection by monitoring the work of businesses and governments and disseminating environmental knowledge to the public The largest environmental NGO in Nigeria, Nigerian Environmental Society (NES), helps to improve the construction process of local infrastructure through professional theory and practice of environmental protection, restoration, and the promotion of environmental sustainability. This could have a direct benefit on improving the environmental situation in Nigeria.

For developing countries, economic development is the primary task of the government, but striking a balance between economic development and environmental protection is also crucial. It is worth noting that adopting the model of cooperation between enterprises and NGOs can effectively help local society to achieve better environmental protection while economic sustainable development. So that Nigeria can achieve a dynamic balance between economic development and environmental protection. A study of Uwafiokun Idemudia indicates the viability and potential of the environmental business–NGO partnerships[41]. This is despite the shortcomings of some of the current cooperative mechanisms, such as the lack of standards for tracking performance. Such cooperation still has great potential to contribute to the achievement of sustainable development on the ground. He also referred to a number of suggestions for cooperation, such as clarifying clear responsibilities, setting measurable targets, and tracking progress.

Future developments and conclusion

As the global economy recovers after the pandemic, some social problems will be alleviated and support for NGOs will increase. NGOs are expected to take further positive action in developing countries to improve the social problems they face for quite some time to come.

NGOs have played an important role in Nigeria's development in various fields. In this

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[41] Idemudia U. Environmental business–NGO partnerships in Nigeria: Issues and prospects[J]. Business Strategy and the Environment, 2017, 26(2): 265-276.

process, the promotion of youth participation and the establishment of local branch organizations are an effective measure to increase impact and practice. In developing countries, where there are often large numbers of new arrivals and young people, involving the youths in solving problems is not just conducive to solving problems. These young people spread the skills and ideas that NGOs have brought to them to continue the positive impact in the society.

The adoption of new technologies and artificial intelligence to improve work efficiency and information processing capabilities may be a trend in the future development of NGOs. Despite the limited economic and equipment conditions in some difficult areas of the developing world, the cost savings, and enhanced benefits of adopting new technologies and artificial intelligence still attract a large number of NGOs.

In addition, the emergence of pro-governmental NGOs highlights the importance of reviewing and monitoring the role of NGOs. NGOs should be more open to public scrutiny, transparent funding, and close contact with the public.

Finally, from the example of NGOs' activities in Nigeria, it can be seen that non-state actors can help developing countries solve many problems. The activities of non-State actors in developing countries need to be taken seriously, actively guided and regulated, and their own capacities and management need to be regulated. It is expected that non-state actors will further interact with various groups in developing countries in the future to alleviate the plight faced by developing countries.

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Water Quality of Residential Lakes vs County-Filtered Tap Water By Sara Kaufman

Introduction–Question

What are the differences in pollution levels (pH, phosphate, nitrate, and microorganism density) between residential lake water and Broward County filtered water in South Florida?

Variables

The independent variable in this study is the source from which the water tested was collected.

The dependent variables in this study are the pH, turbidity, phosphate, nitrate, and microorganism density levels in the water collected.

Controlled variables in this experiment included the amount of water tested, the temperature of the water tested, and the containers in which the water is stored.

Background

Bodies of water surrounded by residential areas tend to have lower qatar quality levels than non-residential bodies of water. This is largely due to runoff and urbanization, especially in residential areas. Storm drains tend to lead into these residential lakes, carrying pollutants from the road (including plastics, road salt, and engine oil) into the water sources. Pesticides and fertilizers used in lawn management can also end up in the surrounding bodies of water, especially if the plants are oversaturated with these chemicals. Formerly, bodies of water had natural filtration systems that purified water as it filtered into the lake or stream. However, the urbanization that has occurred in the past decades (especially near residential areas) has stripped bodies of water of these natural purification systems (*Don't Let Water Quality Go Down the Drain*, 2021).

Water can be artificially filtered for purposes like ingestion and home-use. There are multiple steps to water filtration. First, the water is softened, which involves using lime and ferric chloride to reduce discoloration and hardness (hardness is the amount of dissolved calcium and magnesium in water) (*Hardness of Water*, 2018). Fluoride is then added to prevent consumers' tooth decay. Next, the water is filtered to remove particulate matter, and finally, chlorine and ammonia are added to mitigate microbial growth. Throughout this process, solids that form are pumped into a settling basin away from the main water source (Garcia, 2016).

In Broward County, Florida, tap water is considered safe to drink. The county's water treatment plants focus on two elements of standards: Primary standards, which focus on health-related concerns, and secondary standards, which are concerned with the aesthetic qualities of the water (*Water Quality*, 2021). According to a 2016 report, county water is derived from an aquifer, which possesses natural filtration systems. As mentioned previously, urbanization reduces

the effectiveness of these filtration systems, but the aquifer's location underground reduces how much it is affected by urbanization. In 2016, two water sources in the county (locations 3A and 3BC) had nitrate contents of 0.058 ppm, out of a maximum contaminant level (MCL) of 10 ppm. This contamination was attributed to sewage, the erosion of natural deposits,and fertilizer runoff. Tese and other levels of inorganic contaminants were significantly less than the county's MCL. However, the pollutants identified in that water also included radioactive contaminants and microbes. Prior to March of 2016, water source 3A had a microbe content of 4.9%, only 0.1% from the MCL. After that measurement, increased precautions were taken to properly decontaminate the county's water (Garcia, 2016).

Certain metrics can be tracked to determine water quality, including pH, which is indicative of pollution and can harm organisms living in water By measuring how many hydrogen and hydroxyl ions are in the water, pH tracks how acidic or basic water is (having more ions correlates with a lower pH). pH controls how many nutrients are available for use in water; if a body of water is too acidic (low pH) or basic (high pH) the organisms it affects can die. It is measured using litmus strips, which change color in different pH levels, or probes (*PH and Water*, 2019).

Phosphates and nitrates can also be tracked to measure water quality. Phosphorous and nitrogen are limiting factors that organisms (especially plants) need to grow, and flora can grow exponentially when these chemicals are in usable forms: Phosphates and nitrates. The algal blooms and other plant blooms that arise from an excess of these chemicals can release toxins and deplete the water of dissolved oxygen during eutrophication, killing many animals in that body of water. Much of this surplus is caused by human activities like mining, farming, construction, and sewage management (*Water Quality: Nitrate and Phosphate*, n.d.).

Purpose

In this study, the levels of water pollution in Broward County will be tracked using the aforementioned assays. By comparing the water quality of residential lakes to that of county-filtered water, an indication of residential lake water health will be garnered.

Alternate Hypothesis

Residential lakewater will have higher levels of phosphates and nitrates but lower pH levels than purified water.

Personal Connection

I moved from a big city to a suburban area when I was little. My current home is in a location with a high water table, so there are many lakes interspersed throughout the area. I often visit one of these lakes to watch the sunset and observe marine life. However, I have recently been seeing a lot about water acidification and other forms of pollution in the news. When on the highway, I often pass a water processing plant that dumps chemicals into local waterways, and this form of pollution has high publicity and groups of activists working against it. I am now

curious to see how pollution, especially that from less-recognized sources like roads and lawn fertilizers, also affects local bodies of water like the one I see so often.

Planning-Methodology
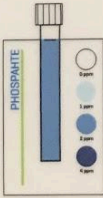
Twenty-five bottles were thoroughly washed with dish soap and water then dried. Four individuals were asked to fill 5 200 mL reusable plastic bottles with approximately 200 mL of water from different points along lakes within walking distance of their houses; at least one of those points was from the section of the lake closest to the nearest road and another one of those was from the section of the lake closest to a landscaped grassy area (like a lawn). The volunteers were instructed to take samples from the top of the lake (to mitigate collecting invertebrates and soil). Five bottles of the same amount were filled with water from 5 Broward County water sinks.

Once all 25 bottles were returned to the lab, they were swirled by hand to ensure mixing of the water inside. pH measurements were taken and recorded for each one using litmus strips (25 data points total). pH measurements were also later taken using a pH probe for increased accuracy. Then, a water testing kit was used to test for samples for nitrates and phosphates (see *Figure 2* and *Figure 3* for testing kit protocol).
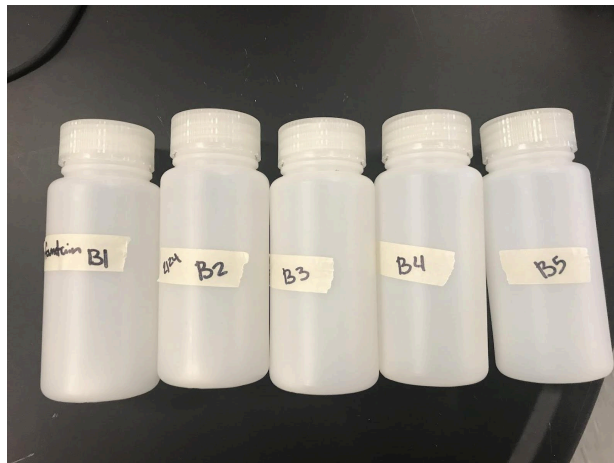
Figure 1 - Labeled bottles used for data collection

Figure 2 - Phosphate testing kit protocol

Nitrate Station
1. Label a clean, dry microfuge tube "nitrate" or "NO_3^-".
2. Pipet 0.5 mL of water from your sample vial into the clearly labeled microfuge tube.
3. Using the O.1 g scoop provided at the lab station, place a half filled scoop of cadmium powder in the microfuge tube containing 0.5 mL of your water sample. Close the lid of the tube and shake well.
4. Add 0.5 mL sulfanilic acid (fill the microfuge tube to 1.0 mL line) to your water sample in the microfuge tube containing cadmium powder. Close lid and shake well.
5. Using a clean pipet, add 5 drops of chromotropic acid to the water sample containing the other two reagents. Close the lid of the vial and shake well. Set this sample aside and record your results at end of class period. The formation of a dark red complex is a positive test result for the presence of nitrate. At the end of class, record your results for this test in the appropriate space in Data Table I, writing either (+) to indicate the presence of nitrate or (-) to indicate the absence of nitrate.

Figure 3 - Nitrate testing kit protocol

Ethical & Safety Considerations

Conducting this experiment involved removing water from local lakes, which may have meant taking water from the habitats of many organisms, and the microorganisms & invertebrates in the water collected would eventually die if the water they were in evaporated. Originally, to prevent both habitat loss and organism death, the samples were to be returned to the lakes they were taken from (taking the samples to a different lake may have caused cross-contamination of disease and introduction of invasive species). However, the samples were left to sit for much longer than planned, and between the potential proliferation of one species and cross-contamination risks, it was decided that the samples should be disposed of. Both the samples and remainders from assays were disposed of according to school protocol.

Handling the samples also posed health risks to the researcher. To prevent acquisition of disease or infection from microorganisms, single-use gloves were worn during testing, and the researcher washed their hands prior to and after handling the samples.

Justification of Methodology

A few elements of this experiment require further justification. Volunteers were used to collect samples because they were using lakes close to their house, which meant that fewer greenhouse gasses were emitted than if the primary researcher collected all the samples (as there was less extraneous driving involved). When collecting water from sinks, different sinks and faucets were used to prevent a potential issue with one of the faucets from skewing the data.

Turbidity was not tested because the samples received were too small/not deep enough to use a secchi disk. While brainstorming procedures, the researcher considered using a spectrometer, but doing so may have ignored green light reflected by algae.

The bottles were cleaned before the samples were collected to prevent dust or other contaminants from affecting the data collected.

The assays used were selected because they most comprehensively measure water quality without surpassing the researcher's financial restrictions (as all materials will be sourced from pre-owned classroom supplies).

Data Analysis

Means were found for each of the values in each lake, and margins of error and standard deviations were calculated. T-tests were conducted among the samples and the control group for each assay. Pairwise comparisons were also taken between the experimental groups.

Observations
- The collector of A samples caught a dead fish in one of the bottles; it was dead prior to their acquisition of the sample
- The researcher dropped a litmus strip in sample D4 but fished it out with a pipe cleaner within minutes; may still have contaminated sample

Data Collection

Note: B was the control sample, taken from sinks.

Raw Data Table

Sample	pH - Probe	pH - Litmus	Nitrates	Phosphates (ppm)
Raw Data Collected				
A1	8.15	7	+	1
A2	7.15	7	-	1.5
A3	8	7	-	1
A4	7.27	7	-	1.5
A5	7.29	7	-	1
B1	7.64	6.5	+	2
B2	7.69	6.5	-	1.5
B3	7.71	6.5	-	1
B4	7.71	6.5	-	1.5
B5	7.73	6.5	-	1.5
C1	7.98	7	+	1.5
C2	7.75	7	+	1.5
C3	8.28	7	+	1.5
C4	7.57	7	+	2
C5	7.41	7	+	1
D1	7.53	7	+	1
D2	7.66	7	+	1.5
D3	7.72	7	+	1
D4	8.15	7	+	1.5
D5	8.29	6.5	-	1.5
E1	8.38	7	-	1.5
E2	8.42	7	-	1
E3	8.46	7	+	1
E4	8.52	7	+	1
E5	8.59	7	+	1

Table 1 - Raw data collected

<u>Data Processing</u>

Averages			
Sample	pH - Litmus	pH - Probe	Phosphates (ppm)
A	7	7.57	1.2
B	6.5	7.70	1.5
C	7	7.80	1.5
D	6.9	7.87	1.3
E	7	8.47	1.1

Table 2 - Average values

Sample Calculation:

Average = sum of values / number of values
D average pH: (7 + 7 + 7 + 7 + 6.5) / 5 = 6.9
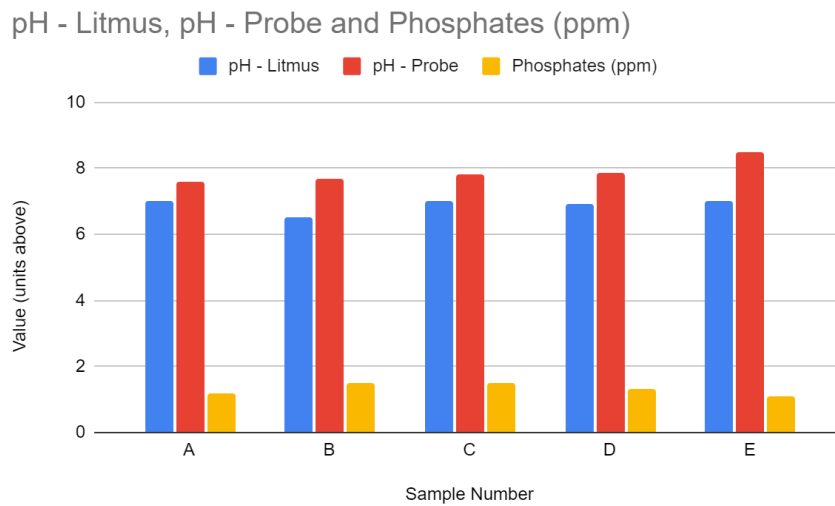
Figure 4 - Average results

Standard Deviations			
Sample	pH - Litmus	pH - Probe	Phosphates (ppm)
A	0	0.47	0.274
B	0	0.03	0.354
C	0	0.34	0.354
D	0.224	0.33	0.274
E	0	0.08	0.224

Table 2 - Standard deviations

Sample Calculation:

$$\sigma = \sqrt{(\sum (x - \bar{x})(x - \bar{x})^2 / n)}$$

Standard Deviations			
Sample	pH - Litmus	0.47 ×)be	Phosphates (ppm)
A	0	=STDEV(C3:C7)	0.274
B	0	0.03	0.354
C	0	0.34	0.354
D	0.224	0.33	0.274
E	0	0.08	0.224

Figure 5 - Sample standard deviation calculation using Google Sheets

Chi Squared Test: Nitrates

Results						
	Control	Experimental				Row Totals
A	1 (0.47) [0.60]	1 (1.53) [0.18]				2
C	1 (1.41) [0.12]	5 (4.59) [0.04]				6
D	1 (1.18) [0.03]	4 (3.82) [0.01]				5
E	1 (0.94) [0.00]	3 (3.06) [0.00]				4
Column Totals	4	13				17 (Grand Total)

Table 3 - Chi square test conducted for nitrate presence

$p = .807$

Therefore, differences are not statistically significant.

T-Test: pH

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T-Test: pH		
Compared	P-Value	Significant (p < 0.05)?
B & A	0.284	No
B & C	0.263	No
B & D	0.138	No
B & E	< 0.0000100	Yes
A & C	0.204	No
A & D	0.138	No
A & E	0.001	Yes
C & D	0.372	No
C & E	0.001	Yes
D & E	0.002	Yes

Table 4 - T-test conducted for pH using probe values

Sample Calculation:

Formula: $T = (\bar{X} - \mu) / S/\sqrt{n}$

Figure 6 - Sample standard deviation calculation using Google Sheets

T-Test: Phosphates

T-Test: Phosphates		
Compared	**P-Value**	**Significant (p < 0.05)?**
B & A	0.0860	No
B & C	0.500	No
B & D	0.173	No
B & E	0.032	Yes
A & C	0.086	No
A & D	0.290	No
A & E	0.272	No
C & D	0.173	No
C & E	0.032	Yes
D & E	0.121	No

Table 4 - T-test conducted for phosphate results

Sample Calculation:

Formula: $T = (\bar{X} - \mu) / S/\sqrt{n}$

Figure 7 - Sample standard deviation calculation using Google Sheets

Conclusion

The initial hypothesis, that residential water would have higher levels of nitrates and phosphates but lower pH levels than Broward County's purified water, was not supported. The control group (samples B1-B5) had slightly higher pH and phosphate levels but lower positive nitrate test results than the other groups. However, after a statistical analysis was conducted, the results gathered were found to only be statistically significant when groups were compared to lake E. The pH levels recorded correlate with previous research, aligning with the United States Environmental Protection Agency's freshwater pH range of 6.5 to 9 (Environmental Protection Agency, 2023). Additionally, a 2019 county-sponsored report states that Broward's nitrate levels are only approximately 0.3 ppm, meaning that they are present (albeit in low quantities), which also correlates with this study's results (*Water Quality Water Quality Report for 2019*, 2019). County phosphate levels have been shown to be about 0.02 mg/L, which is starkly lower than the levels reported in this study (Dunn, 2001).

Evaluation

Though this study provides a foundation for water quality testing, it is not comprehensive. By only considering three assays, it neglects other indicators of water quality, like indicator species and pollution levels. Additionally, some potential sources of experimental error that could have led to the higher P values and standard deviations have been listed below.

- The bottles were initially washed using tap-water that may have been contaminated or affected the final results.
- The nitrate data was collected using colors, which are harder to read and less precise than numeric values; pH levels were originally also taken with this method until a probe was later acquired
- Once the pH probe was acquired, the pH levels were re-taken. However, the water had been sitting in bottles for varying numbers of days by then, so that variable was no longer controlled. Some pH levels may have changed due to the increase or diminishment of microorganisms in the water.
- Cross contamination may have occurred, as the same syringe was used across samples when taking phosphate levels and the same probe was used to record pH levels.

Concerns have been raised about using a t-test instead of an ANOVA test to evaluate the results' statistical significance. However, there is no "minimum" number of data points for a t-test. The first t-test run only had 4 trials per group (compared to the 5 used in this study); therefore, the t-test is a reliable evaluation of the results' validity (Zach, 2021).

Application

This study provides the foundation to better understand water contamination in Broward County residential lakes. By comparing the water quality of residential lakes to purified water, scientists can consider how effective the purification process is. They can also learn about the residential lakes' contamination levels and re-evaluate the use of substances like pesticides and placements of roads near water.

However, it is important to note that human behavior is hard to change, so though these results demonstrate a need to limit the use of chemicals like pesticides near residential lakes, they will likely not lead to the actual resolution of lake pollution. These changes would have to be incentivized, likely with a monetary reward for avoiding those chemicals.

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Evolution of Genetic Engineering in Medicine: Recombinant DNA and CRISPR Gene Editing Technologies By Manasvi Jambula

Abstract

Genetic engineering is a new and upcoming field constantly developing. This field has so many possibilities and opens up new doors for ideas and solutions we have not seen before. Gene editing allows us to make edits, deletions, and substitutions in sequences. Recombinant technologies allow us to use aspects of other organisms' DNA. Gene editing technology has the potential to improve or possibly reverse symptoms of inherited or acquired genetic diseases. There are two predominant modes of genetic engineering in medical biotechnology: recombinant DNA and CRISPR gene editing. Recombinant DNA technology uses another organism as a host to create the desired outcome for the source. To perform edits using CRISPR, the utilization of recombinant technologies is important. Recombinant DNA technology allowed for the manipulation of sequences while often using hosts like bacteria. CRISPR-mediated gene editing is a technology that has grown from and is also partially dependent on recombinant DNA technology. Gene editing is constantly evolving and adapting to new needs and possibilities. There are many promising discoveries and the ongoing development of recombinant and gene editing technologies allows for new possibilities and future advancement in medical biotechnology. I will review recombinant DNA technology and its development into CRISPR gene editing technology in this article and then describe several real-world applications of these technologies to improve human health.

Recombinant DNA technology

The foundation of medical biotechnology is recombinant DNA. This subfield was a transformative point in DNA technologies, which propelled newer more advanced technology. Recombinant DNA technology was developed in the 1970s by Paul Berg, Stanley Cohen, and Herbert Boyer at Stanford University. Recombinant DNA technology was the genesis of genetic engineering in not only medicine but agriculture as well (Gill et al., 2023). Recombinant DNA works by isolating a specific gene or parts of DNA from one organism and inserting them into the DNA of another, allowing scientists to combine DNA from different host sources and generate new compositions of DNA that wouldn't occur naturally. This process can apply to different species and organisms. Recombinant DNA technologies are growing in many fields, like medicine and agriculture.

There are several steps in creating recombinant DNA. First, the desired DNA fragment, which encodes for a protein, is isolated from a donor species via polymerase chain reaction (PCR). Invented in 1983 by Kary Mullis, PCR works to rapidly copy and amplify a targeted piece of DNA repeatedly (Kaunitz et al., 2015). Next, restriction enzymes, or other techniques, assemble the fragments. Enzymes like DNA ligase are used to "glue" the fragments together. Restriction enzymes cut DNA at specific sequences. Using polymerase chain reaction and restriction enzymes, the fragment is isolated and cut. The DNA fragment is assembled into a circular construct known as a plasmid. This allows for the replication inside of a host species,

commonly yeast or *E. coli*. The recombinant plasmids are then grown up. The copies inside the host species are purified. Lastly, the recombinant DNA is introduced into the host organism, where the plasmid is transcribed and translated to produce the desired protein (Figure 1). There are numerous ways for the DNA to be inserted back into the host such as electroporation, microinjection, virus transduction, or lipid nanoparticles. The technological development opened new doors and possibilities.
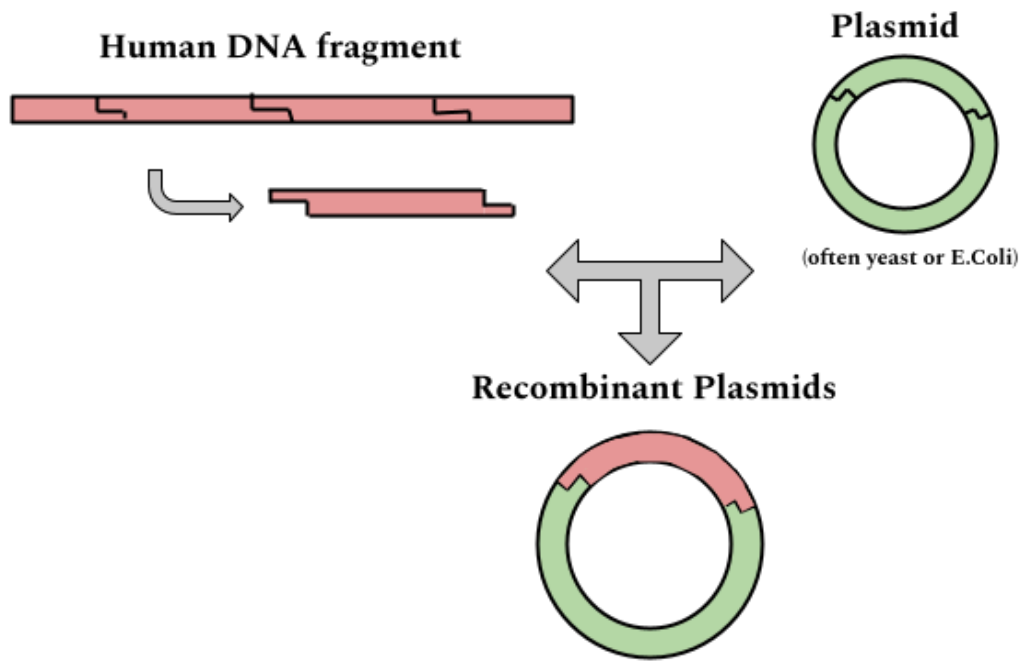
Figure 1. The desired DNA fragment, or trait, is amplified from a donor species via PCR. Restriction enzymes or other techniques are used to assemble the fragments. Using PCR, the fragment is isolated and cut. The DNA fragment is assembled into a circular construct known as a plasmid. Replication occurs inside a host species, commonly yeast or *E. coli*. Then, the recombinant DNA is introduced into the host organism, where it's replicated and produces the desired trait or protein, such as insulin.

Going back to the first step in creating recombinant DNA, Polymerase Chain Reaction works to copy and amplify a targeted DNA segment repeatedly. PCR requires the DNA you intend to make copies of, DNA primers, nucleotides, and heat-resistant DNA polymerase enzymes like taq polymerase, as outlined in Figure 2.
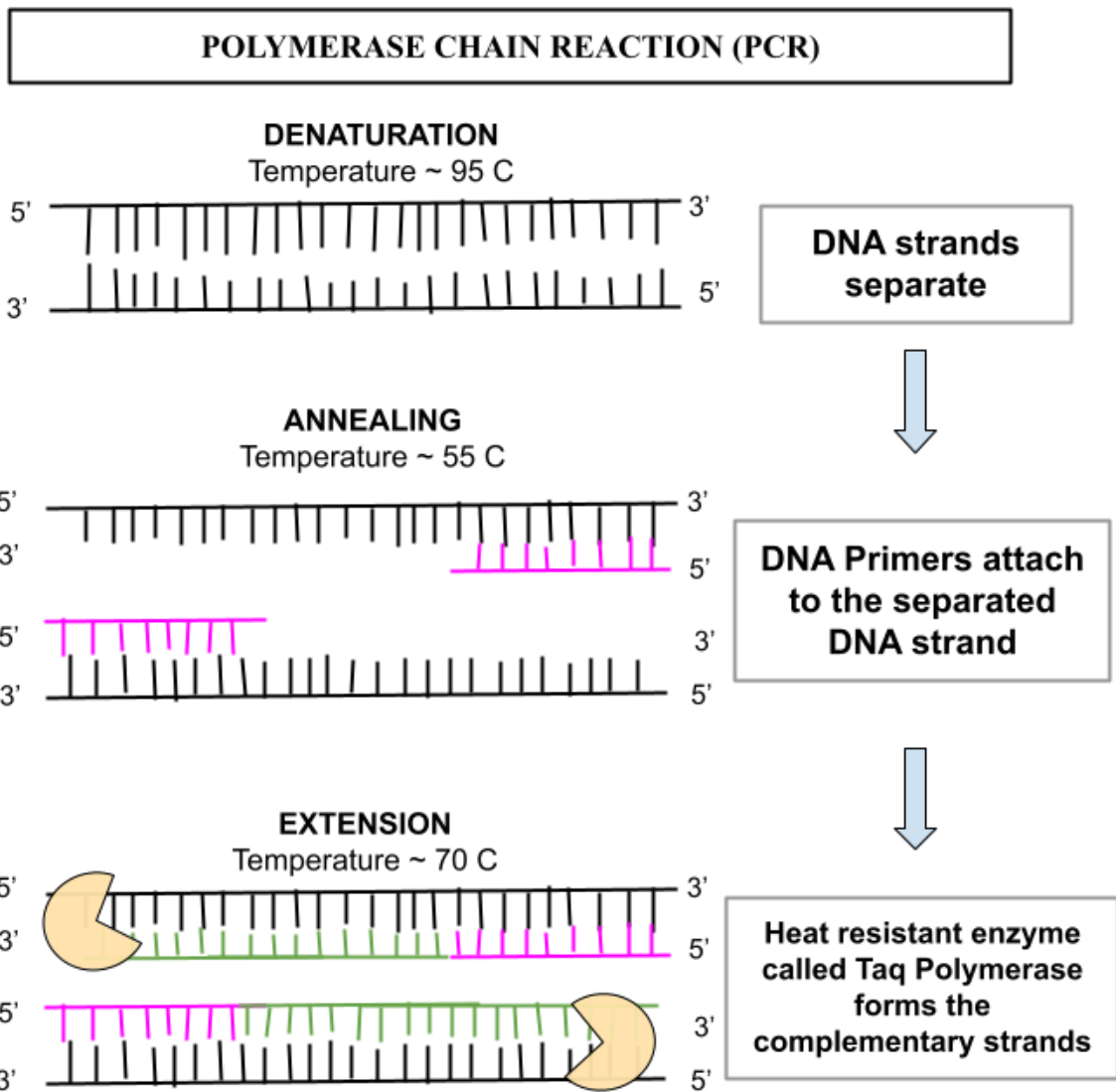
Figure 2. Overview of PCR. To begin, the first step involves denaturing which causes the double helix structure to untwist and separate at the base pairs. Next, the two strands that normally form the double helix separate due to denaturing or "melting". Denaturing in this case means to heat the DNA sample to a high temperature that breaks the hydrogen bonds present between nucleotides on the opposite sides of the strands. The next step, which is called annealing, lowers the temperature. During this step, short sequences of DNA called primers, which are complementary to the base pairs, bind to the complementary sequences on the single-stranded DNA. Lastly, in extension, the temperature is raised once again. A DNA polymerase enzyme like Taq polymerase is then used to synthesize or create a new DNA strand complementary to the single-stranded template (Zhu, 2020). This results in two new double-stranded DNAs that match the original target DNA fragment. When the reaction is repeated, those two pieces double to 4, and so on.

The simplicity and productivity of PCR have made it a vital tool for various uses and it continues to be essential in many critical applications such as diagnostics, fingerprinting, and virus detection. Polymerase chain reaction has transformed so many fields. Although the main focus is DNA amplification, as it can amplify DNA at rapid rates and efficiently, there are many uses for PCR. These applications allow scientists and researchers to synthesize functional DNA constructs to produce a product of interest inside of the host. Some of the main applications seen throughout other fields are genetic research, mutation detection, environmental science, medical research, forensics, and the development of medication and drugs (Zhu et al, 2020). Recombinant DNA is utilized in numerous areas of medicine and biotechnology. A prominent example is synthetic insulin for the treatment of Type I diabetes. In the 1920s, when insulin was first discovered as a treatment for diabetes, the hormone had to be extracted from live, non-human animals. This process of procuring naturally-produced insulin was time-consuming and laborious, yet it remained the standard practice for nearly 50 years (Quianzon et al., 2012).

In the late 1970s, Herbert Boyer and a team of scientists from the University of California San Francisco and Stanford University used recombinant techniques to develop synthetic insulin. PCR was not developed at this time as it was later invented in 1983. Researchers assembled the entire insulin gene sequence using 3-base-pair fragments, one at a time in a specific order. Next, they incorporated this into a plasmid using restriction enzymes (Beutler, 1978). This required inserting human insulin-encoding DNA into yeast or bacteria cells. These cells can then be grown to high numbers and instructed to produce human insulin which could be then isolated from organisms and used in human patients (Vajo, 2001). This large-scale application of recombinant DNA technology to the medical field laid the foundation for what would become one of the nation's most prolific biotechnology companies: Genentech. The use of genetic engineering to produce synthetic insulin afforded a more consistent, safer, and scalable drug development process. Importantly, the use of synthetic insulin hormones eliminated the risk of adverse, allergic reactions that were associated with animal-derived insulin (Quianzon et al., 2012).

Indeed, Boyer's achievement at Genentech was a major milestone and changed the treatment of diabetes immensely (Quianzon et al., 2012). As recombinant technology further developed it opened the possibilities for novel, more targeted treatments in which specific properties of a drug could be tailored to a patient's needs. This resulted in increased drug effectiveness and safety.

Similarly, vaccine development has been enhanced by recombinant technology. Traditionally, vaccines require involved use of weakened or attenuated forms of a whole pathogen. Recombinant DNA technology enabled the production of subunit vaccines, whereby only select proteins or antigens from the pathogen are supplied by the vaccine rather than the whole form. This removes the risk of virulence or infection upon vaccination while maintaining the desired immune response (Nascimento et al, 2012).

Another application of recombinant technology is in diagnostics. Diagnostic tests are used to detect the presence of pathogens or disease biomarkers in a patient sample such as blood or

urine. Recombinant technology aids in this detection by identifying the specific binding sites in which antibodies bind to antigens (Ebrahimi et al, 2022). Advanced tools like these have shown great potential. These technologies have not only revolutionized research but have pushed to open a range of wide possibilities.

Although it primarily focuses on treating genetic disorders, an alternate approach provides patients with "treatment" not a permanent cure. Recombinant DNA technologies work in mitigating and managing the symptoms. More advanced technologies like CRISPR-Cas9 have the potential to possibly cure genetic diseases by making direct edits to the DNA fragment within the genome of the host organism. The crucial transition between recombinant and editing technologies is the idea of treatment vs cure. Both technologies have had a significant impact and are constantly developing.

CRISPR-Based Gene Editing

Gene editing and recombinant DNA technology are both approaches to biotechnology, the two have developed and grown off of each other. Gene editing is a more precise, targeted approach to modifying specific areas of the genome. Gene editing is a molecular biology technique that is used as a powerful tool to get more specific and targeted modifications of an organism's DNA. It allows for the modification of a specific sequence with precision and accuracy. Gene editing is altering a living organism by replacing, removing, or adding a DNA sequence to improve or correct something (Doudna, 2020).

One of the most central forms of gene editing is CRISPR-Cas9. "CRISPR" stands for Clustered Regularly Interspaced Short Palindromic Repeats and "Cas9" means the CRISPR-associated protein 9. CRISPR technologies evolved from fighting viral DNA in bacteria, an immune system in bacteria, to being modified for all DNA types. CRISPR-Cas9 was a revolutionary piece of gene editing technology. The beginnings of CRISPR go back to the 1980s when a research team led by Yoshizumi Ishino discovered repetitive DNA sequences in *E. coli*. Later on in the 2000s, Francisco Mojica also started noticing repetitive sequences. In 2005, Philippe Horvath and Rodolphe Barrangou found CRISPR sequences and connected the idea to bacterial immune response. Then in 2012, Jennifer Doudna and Emmanuelle Charpentier discovered that the Cas9 protein could be programmed with an RNA molecule to target specific DNA sequences (Jinek et al., 2012). This opened up numerous possibilities for the use of CRISPR-Cas9. To build on this, in January 2013, Feng Zhang, who was a researcher at the Institute of MIT and Harvard was the first to adapt CRISPR-Cas9 for editing in eukaryotic cells such as humans (Cong et al, 2013).

Many have found this technology exceptionally remarkable due to its capability to act as molecular scissors (Figure 3). For a CRISPR gene edit to proceed, the researcher must first identify the specific sequence of DNA that they desire to edit and then design a guide RNA that matches the target sequence to tell the Cas enzyme where to cut. CRISPR can act as a "scissor" and make a simple cut. It relies on the gRNA which is designed to match the DNA sequence

being modified. The gRNA and Cas9 protein are then introduced to the cell and gRNA guides the Cas9 to where the edit needs to be made (Swartjes, 2020). The Cas9 "scissor" then makes the cut and the ends are joined again. To further describe the "edit", gRNA directs the Cas9 where the cut will be made and the cell has repair pathways that fix the "cut" in the DNA. One of the pathways is non-homologous end joining which is error-prone. When errors occur, things like mutations can be introduced which disrupt the normal function of the gene and can lead to a non-functioning protein (Gostinska, 2022).
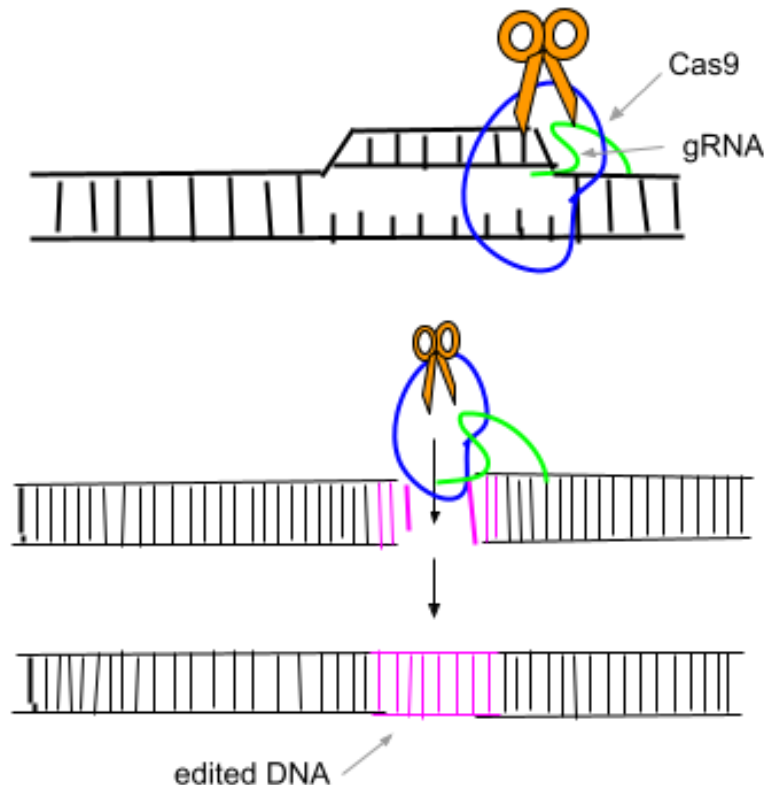
Figure 3. A guide RNA guides the Cas-9 where to cut. The cell itself repairs the cut in a way that leads to a change in the DNA. The Cas-9 protein acts as "molecular scissors" and can make edits efficiently and directly.

Similarly, single base edits involve making a change in a single base, for example changing a cytosine to an adenine. Importantly, base editors utilize a variant of Cas9 that is often "kinase-dead" which prevents them from cutting through both strands. The base editor converts the targeted base to a different base pair which creates a single base pair without affecting the surrounding sequence (Yadav, 2020). To summarize, CRISPR/Cas9 can be used to create a targeted mutation in a sequence, add new genetic information, or perform very precise edits to change the DNA sequence in a targeted way. These strategies have opened the door for many real-world applications of CRISPR gene editing, as will be discussed in the following section.

Applications of CRISPR gene editing

CRISPR is being used to test for COVID-19 RNA. The test is conducted by first acquiring a respiratory or nasal sample from the patient. The RNA from the sample is extracted to test for the presence of COVID-19 (Avery et al., 2022). Reverse transcription is used to convert RNA into DNA so that the CRISPR/Cas9 complex can recognize it. The DNA is amplified through polymerase chain reaction. CRISPR-Cas9 system uses a gRNA which is designed to use a specific sequence of DNA if it is present. If the gRNA encounters the target sequence, the CRISPR-associated enzyme is then guided there to the target sequence. When the CRISPR system has binded to the targeted area it activates the cleavage activity which then cuts a reporter molecule that releases a fluorescent signal which signals the detection of viral DNA. The absence of fluorescence is usually an indication of no viral DNA, and the presence of fluorescence indicates positive viral DNA results. Recently, this method has been further developed into a more direct CRISPR-based test that doesn't require reverse transcription and instead uses Cas proteins to identify and cut RNA instead of DNA (Gaanbatar, 2021).

Another application of CRISPR gene editing is to treat sickle cell anemia. Sickle cell anemia is caused by a single nucleotide mutation in the hemoglobin gene, resulting in abnormal hemoglobin. This causes the red blood cells to become deformed and less flexible (Martin et al., 2006). CRISPR technologies can first target the hemoglobin gene and directly modify the faulty gene. In sickle cell anemia, the goal is to specifically target the mutated gene that is the cause of the abnormal hemoglobin being produced. Then the CRISPR-Cas9 binds to the location, and the Cas9 enzyme cuts out the DNA at the specific area. After its cut, the cell can naturally repair the cell. Similarly, another approach to CRISPR involvement in sickle cell includes targeting a negative repressor fatal hemoglobin instead of the mutant gene itself (Park,2021). A repair template is then needed to "fix" the break in the DNA which allows for any mutation to be corrected. This is a new field of opportunities, and it's currently being researched regarding its effectiveness and safety.

Huntington's disease is also an area with potential applications for CRISPR. Huntington's is a neurological disease caused by a mutation in the Huntington gene. The mutated Huntingtin protein builds up in the brain, which leads to progressive damage in the nerve cells, and it causes other cognitive and psychiatric problems. Similar to the process of CRISPR being used in sickle cell, first, it targets the gene or the mutated region. The gRNA binds them to the targeted area and then cuts the DNA, forming a double-stranded break. The fix uses DNA repair systems as mentioned previously, to insert the sequence for normal Huntingtin protein production. The result is that cells no longer produce the mutant protein, which could reverse the pathology of the disease. A challenge particular to this condition is its complexity which requires delivery of CRISPR/Cas9 system to the brain tissue which is impossible or extremely invasive. In contrast, when treating something like sickle cell, you must edit blood cells which can be acquired through draw or marrow and then reintroduced to a patient (Park, 2021). Current efforts and research are being directed to explore delivery methods that are not as invasive such as lipid nanoparticles or antibody-directed approaches.

Ethical Implications of Genetic Engineering in Medicine

Many issues can occur in gene editing. Pleiotropic effects occur when a change to one element impacts the functionality of some seemingly unrelated function. This relates to the debate of whether new advancements in gene editing are safe for humans. A single change can have other off-target effects on the rest of the genome. Changes like insertions, deletions, and substitutions can have other unanticipated effects. CRISPR-Cas9 can be used to make edits at specific parts of the DNA. Off-target editing can occur even with technologies such as CRISPR-Cas9. An off-target sequence can be recognized by the CRISPR/Cas9 and it can cause unexpected edits and potential mutations in the genome. Specifically, if the off-target site is in a growth factor receptor it can promote cancerous growth.

Many ethical concerns have also risen in the debate on whether or not gene editing is okay to implement. Many ideas like consent, medical problems, future effects, inequality, positive medical potential, and unintended effects are critical in the debate regarding ethics and hesitancy (Joseph, 2022). A concern that comes up in the debate is the effect on future generations, it debates whether or not the genetically modified effects should pose a concern to the next generation inheriting them. Changes in genetic material that is passed down have concerns like safety as well as consent. It raises questions on long-term impacts that we haven't fully assessed and have not been tested yet. On one hand, equal access is another key point that has repeatedly been brought up, people question if genetic modifications should be allowed if they are not equally accessible to all levels of social class. Since not everyone can afford this relatively new and pricey technology, it is unfair for people of the richer class to be able to genetically modify a genome (Joseph et al, 2022). Regulation and consideration are imperative in balancing scientific evolution and ethical concerns. Similarly the term "designer babies" is an umbrella term for talking about creating offspring that are genetically modified or edited for specific traits, it also raises numerous ethical questions and challenges on what it means to have diversity and express human values. Many believe that humans should not be genetically altered because they have been biologically created to be unique and person (Gostinska, 2022). However, genetic modification has been showing promising results for many fields of medical biotechnology, with new solutions that would not have been possible otherwise. Others argue that gene editing should be used solely for medicine and health (Gostinska, 2022). Genetic engineering has the potential for finding cures and new research for disease, illness, and even personalized medicine.

Conclusion

Overall, the field of medical biotechnology has encompassed a vast area of possibility and development and achieved numerous milestones in science, genetics, and medicine. Medical biotechnology constantly evolves through advancements such as insulin advancement, CRISPR-Cas9, and more precise technologies. Although there are many upcoming advances and discoveries this topic still raises futuristic questions relating to ethics, acceptability, and impact

which are all important to consider. Rapidly advancing ideas and work are opening up new research to cures for genetic diseases, cancer therapies, neurological disorders, and even enhanced human traits. Though there are medical and ethical concerns, advancements could lead to newly progressing technologies and applications. Gene editing continues to evolve and grow to new levels while simultaneously adapting to individualized projects and research.

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Electric Vehicles and Internal Combustion Engine Vehicles: A Quantitative Comparison By Vidit Aggarwal

Abstract

This research displays quantitative analysis on the shortcomings of both battery electric vehicles (BEV) and internal combustion engine (ICE) vehicles. BEVs are lacking in fundamental concepts such as price, range, charging time and infrastructure, whereas ICE vehicles completely outclass them; however, ICE vehicles fall behind BEVs in terms of energy efficiency and unsafe emissions. These properties together form two major problems for BEVs: range anxiety and slower adoption into underdeveloped countries. These quantities allow us to understand the reasoning behind the chicken-egg cycle for the lack of infrastructure and the lack of BEVs, one causing the other. The potential of solar cars was also discussed as they could, with better efficiency, solve most of the problems with BEVs and achieve reduced charging events.

Introduction and Motivation

The automotive industry is a key component of every country's economic growth. This industry provides cars each year that are safer and faster, supplementing the transportation network and making it easier for human and cargo transportation. This growth does not come without its consequences: the rising pollution from these cars accounts for about 29 percent of total U.S. greenhouse gas emissions (United States); these emissions trap the warm air inside the atmosphere and increase global warming. While promoting the growth of the automotive industry, it is also of importance to keep the environment in mind. As such, battery electric vehicles (BEV) have shown tremendous potential, as they produce zero tailpipe emissions.

Despite this benefit, BEVs still struggle to sell in comparison with their gasoline counterparts which have better range, much faster refueling times, better performance, and a much better infrastructure. Most of the infrastructure was developed after 1920 ever since Henry Ford industrialized the production of gasoline cars. BEVs still lag behind in all these areas, especially in infrastructure, which seems to be stagnant due to the lack of BEVs; the lack of BEVs contributes to the lack of infrastructure. This cycle seems to be never ending, especially when it comes to countries still in their developing stages (Alanazi).

As these countries develop, BEVs will start to replace ICE vehicles due to their benefit of zero tailpipe emissions. As ICE vehicles get replaced, more and more BEVs will siphon major electricity from the power grid ranging from 1kW to 350kW; this would result in an immense load on the grid, and instability events in power grids are unacceptable to society. The consequent blackouts can cause huge economic losses and can even threaten the security of a society (Liu et al.). The fundamental problem with these vehicles stems from the quantitative features of the vehicle such as their range, recharging process, and high cost. With the help of scientists and their research, technological advancements can be made in battery technology and infrastructure costs to make vehicles independent from the power grid.

Recent advancements ranging from the blade battery technology presented by BYD—a BEV manufacturing giant in China—to solar powered cars by Sono Motors and Lightyear means that there is active research in this pace leading to new technological advancements. The primary goal of these Original Equipment Manufacturers (OEMs) is not only to increase the range and decrease the charging times but also to reduce the price and pollution caused by these vehicles both directly and indirectly.

Developed countries have a higher percentage of renewable energy in their energy generation compared to underdeveloped countries which prefer cheaper power generation methods due to poverty. Currently, 65% of the overall pollution generated from a BEV in the USA is from its energy source (United States Environmental Protection Agency), this is even higher for underdeveloped countries. To fully realize the potential benefit of zero pollution from BEVs, having a clean energy source plays a vital role.

Underdeveloped countries such as Afghanistan and Bangladesh cannot adopt BEVs due to ongoing problems such as soaring debt, energy poverty, export marginalization, and climate vulnerability to name a few (UNCTAD). These problems prevent them from spending extra on the higher upfront costs of BEVs; therefore, BEVs should be technologically advanced enough to outperform a traditional vehicle in all aspects.

Range anxiety is the fear of running out of electricity. BEVs owners are extremely susceptible to range anxiety; electricity to charge a BEV cannot be externally stored—external batteries don't have the capacity to recharge a BEV to a significant level—and BEVs have much shorter ranges as compared to ICE vehicles. This problem needs to be addressed since BEVs struggle with long road trips; if you are unable to locate a charging station in time, the car will shut off.

The overall goal of this research is to provide recommendations for a more reliable and futuristic solution that can be provided with the vehicle itself rather than relying on the government to encourage buyers with incentives and other such methods. This can be beneficial for both the OEM and the buyer, resulting in smoother adoption of BEVs.

Methods

The two countries that will be compared are the USA—a global superpower, with the current dominating currency—and India. India has been chosen due to high rates of growth in its economy worldwide, making it suitable for observation in the coming years (Patnaik and Pundit) along with its dire need for environment-friendly vehicles, that stems from housing the largest population in the year 2023 (Hertog et al.).

The selection of ICE (Internal Combustion Engine) vehicles was done by sorting the highest selling brands (Carlier). From these brands the highest selling sedan and SUV were chosen for the calculation of raw data. For BEVs, the company's sales were disregarded, and the cars were chosen based on the most units sold nationwide. The selection of cars was done for two categories: India and the USA. Each of these categories had further two subdivisions: sedans and SUVs. Each division consisted of four cars.

Price: The comparison of the price of cars was calculated from the average price of each category, and the averages were then compared against their fuel-based counterparts, with sedans being compared to sedans and SUVs being compared to SUVs. The upfront retail price of each car was sourced from the OEMs official website.

Range: This metric compares the range of the BEV against the range of a traditional ICE vehicle. Data was calculated in a similar way to the price by averaging the range of the selection of cars and making a direct comparison with the values. The data source was primarily the brand's website itself; however, in some cases an alternative generalized website was used. The calculation of range was done by three standard tests: NEDC, WLTP and EPA. Due to the collection of data from a variety of different websites, all the cars did not undergo the same test and thus may be a bit inconsistent.

Refueling/Recharging Times: This comparison is between the recharging time of a BEV and the refueling time of gasoline-based cars. The recharging time for a BEV can vary a lot based on the wattage output of the charger; therefore, a standard of Level 2 (240V AC) charging was assumed, as these are the most common chargers in both recharging stations and household chargers. This was calculated by using the average recharging times of BEVs in their respective categories and with a common gasoline refueling time of 2 minutes for sedans and 3 minutes for SUV to account for the larger fuel tank sizes of SUVs.

Density of Stations: The density of stations was calculated by averaging the density of stations in a metropolitan city and urban city; the density for each city was calculated by dividing the number of stations by the area of the city in square miles. The primary reason in choosing a metropolitan city stems from the large population it houses and the high income households it houses which are most likely to purchase a BEV (Davis). Urban cities were chosen because it is challenging to find viable data for rural towns, areas with low population density, especially in India where most rural towns have no charging stations at all.

Energy: This metric consists of three different comparisons. First, the cost of one kilowatt-hour of electricity sourced directly from the power grid and one kilowatt-hour of fossil-fuel based energy (petrol since most of the selected models of cars use petrol) was compared. This factor was calculated and compared separately for India and the USA, due to the difference in availability of fuel which causes a difference in cost. Secondly, a comparison between the percentage of energy that was converted into useful energy between BEVs and ICE vehicles was directly sourced from online sources. The third comparison was a combination of the first two, where the cost of the distance traveled on one kWh of energy was compared between BEVs and traditional gasoline vehicles. The data was sourced from the first two comparisons and was mathematically calculated by multiplying the percentage by the value of the first metric.

Results

Figures of Merit	INDIA	USA

	Real values	Normalized	Real values	Normalized
Price of BEV sedan : Price of ICE sedan	35,074.02 : 9,257.50 [USD:USD] (converted from INR to USD at 1 INR = 0.12 USD)	3.78:1	34,655 : 25,625 [USD:USD]	1.35:1
Price of BEV SUV : Price of ICE SUV	27,190.77 : 12,817.56 [USD:USD] (converted from INR to USD at 1 INR = 0.12 USD)	2.12:1	48,307.5 : 30,661 [USD:USD]	1.58:1
Range of BEV sedan : Range of ICE sedan	294 : 494 [miles:miles] (converted from km to miles)	0.59:1	267.25 : 493 [miles:miles]	0.54:1
Range of BEV SUV : Range of ICE SUV	278.5 : 573.33 [miles:miles] (converted from km to miles)	0.48:1	284.5 : 452.4 [miles:miles]	0.63:1
Charging of BEV sedan : Refuelling of ICE sedan	7.7 : 0.033 [hours:hours]	233.3:1	7.75 : 0.033 [hours:hours]	234.8:1
Charging of BEV SUV : Refuelling of ICE SUV	9.9 : 0.05 [hours:hours]	198:1	6.5 : 0.05 [hours:hours]	130:1
Density of Charging Stations : Density of Gas Pumps	1.71 : 2.51 [No. per sq.mile: No. per sq.mile:]	0.68:1	18.31 : 1.95 [No. per sq.mile: No. per sq.mile:]	9.36:1
Price of Electricity per kWh : Price of Petrol per kWh	13 : 7.7 [cents:cents]	1.69:1	13 : 16.7 [cents:cents]	0.78:1
Price of Electricity per useful kWh of energy : Price of Petrol per useful kWh of	10 : 61.90 [cents:cents]	0.16:1	21.69 : 61.90 [cents:cents]	0.35:1

energy				

Table 1: A numerical representation of the data collected and the figures compared (https://shorturl.at/AMORT)
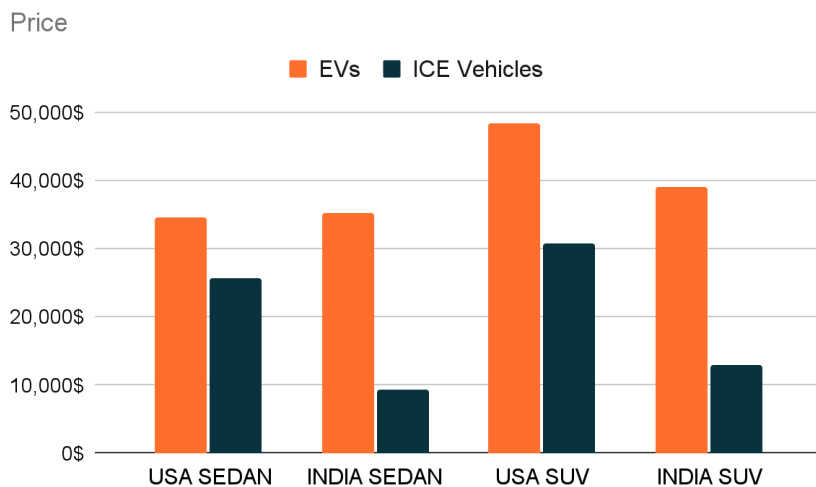
Price

Figure 1: Representation of the average price of vehicles in dollars
Figure 1 shows the average prices of the selection of cars. This depicts the difference between ICE vehicles in both the countries and highlights the importance of price to increase selling in low cost of living countries.

Range (miles)
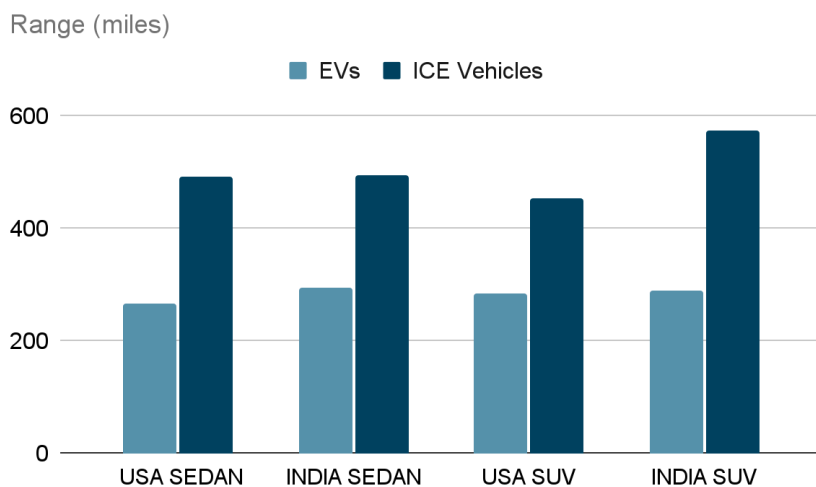
Figure 2: Representation of the range of a vehicle in miles
Figure 2 compares the average range of vehicles in their respective categories. This is used to highlight the significant differences between BEVs and ICE vehicles. It also shows the similarities between entirely different OEMs in different countries.

BEV charging time	sedan	SUV
a. USA	7.75 Hrs	6.5 Hrs

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b. INDIA	7.7 Hrs	11.125 Hrs
Fossil Fuel refueling time	0.033 Hrs	0.05 Hrs

Table 2: Representation of the charging times of BEVs and refueling times of gasoline based vehicles

Density of Station (Stations per sq.mile)
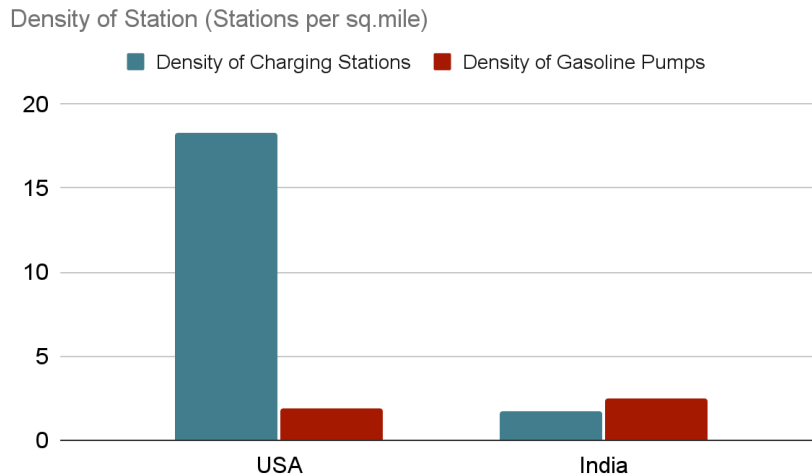
Figure 3. Represents the number of stations per square mile in highly populated areas

Figure 3 shows the density of stations on average in the respective countries. Its main purpose is to show the difference between a developed country and a developing country by highlighting the significant difference between the density of charging stations.

Cost per of kWh of Energy Source
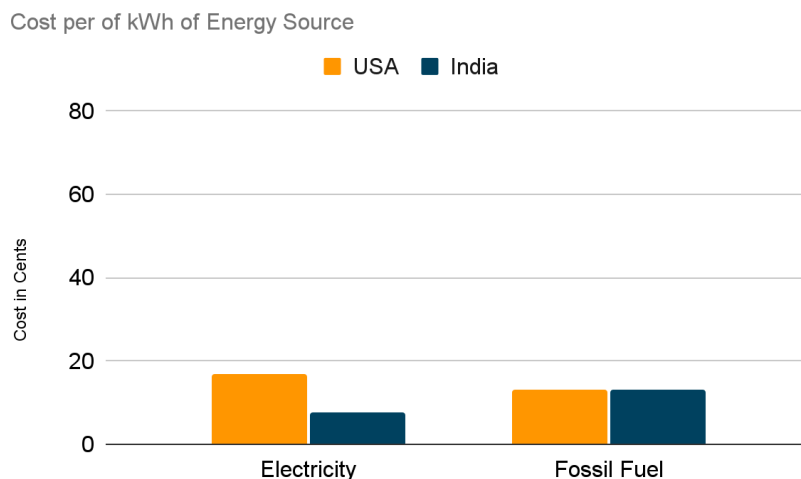
Figure 4: A comparison between the cost of electricity

In Figure 4 the first graph represents the cost of one kWh of energy in the USA and India between fossil fuels and electricity supplied directly from the power grid. The second graph depicts the cost of 'useful' energy – energy used in moving the car – for the respective vehicles. This cost was derived from the efficiency of the vehicle – which refers to the energy conserved for the wheels after factoring in energy loss from various sources: heat, friction and other accessories such as speakers – this was typically around 77% for BEVs and can range between 12-30% for ICE vehicles (US dept. of Energy)

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Analysis and Discussion

      The results from the collection of data have highlighted a series of factors which indicate the reasons for the slow adoption and subpar selling of BEVs in developing countries, in this case India. The comparison of India to the US, assists us in separating factors that may have affected the data such as higher cost of living.

Price

      Price is the most important factor when comparing cars; approximately 42% of buyers in 2022 stated this to be the largest factor considered when making a purchasing decision (Autolist Editorial Staff). It can be concluded that BEVs have a higher upfront cost. Electric sedans are 35% more expensive than ICE sedans, and electric SUVs are 58% more expensive than ICE SUVs (See Figure 2). This increase in price makes BEVs unfavorable to the majority of low income households, especially in India where low and middle income households make up a majority of the population and only 3% of the population made over $3600 annually in 2021 (Rathore). While this is enough to sustain an adequate life in India, it is in no way enough to purchase a BEV that retains similar upfront costs to the US. The large contingent of the low and middle income households also support the data from Figure 2 where Indian ICE vehicles are only a fraction of the US ICE vehicles; this is a result of adaptation in a low income environment, and BEVs have yet to see this form adaptation and revolution.

Range

      Range is a core performance measure for every car, and approximately 39% of buyers in 2022 stated range as their second biggest concern when making a purchasing decision (See Figure 3). ICE vehicles almost doubled their respective counterparts in terms of range. This difference in range can be attributed to their smaller energy capacity, as the average BEV has a storage of only 60 kWh and up to 75 kWh for SUVs (IEA) as compared to ICE vehicles that can store up to 50-60 L of fuel (Wikipedia contributions). Therefore, since one liter of petrol contains 8.9 kWh of energy this amounts to 445-534 kWh of energy in the average fuel tank which is several times more than BEVs, this displays the huge gap in storage capacity that BEVs still have to make up. This gap is extremely difficult to make up due to a variety of reasons, which stem from the chemical composition of the battery.

● Low-nickel ● High-nickel ● LFP ● Other
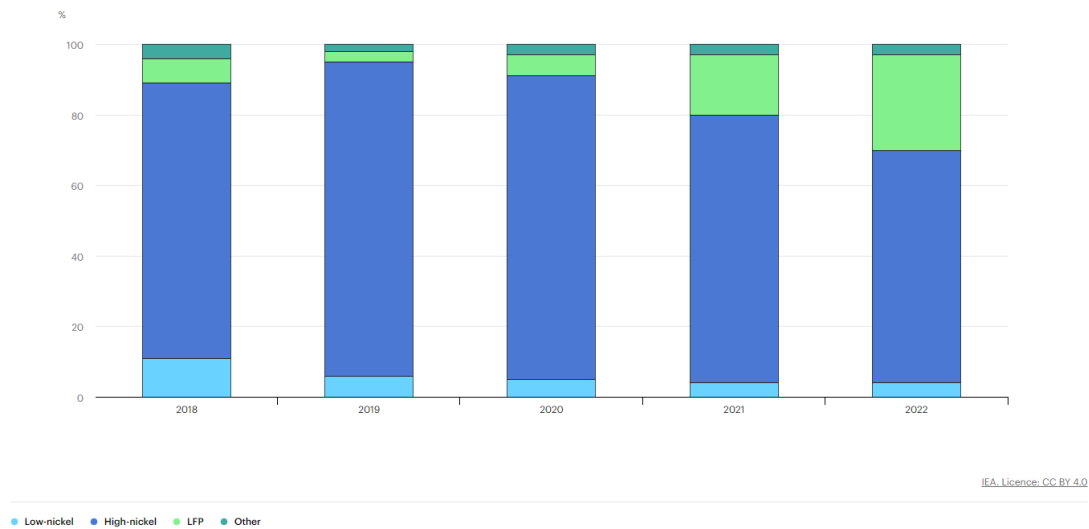
Figure 5: Chemical composition of batteries by IEA:
https://www.iea.org/data-and-statistics/charts/electric-ldv-battery-capacity-by-chemistry-2018-20
22

Lithium nickel manganese cobalt oxide (NMC) has been the most common choice for the battery, with a market share of 60% due to its high energy density. The second most common choice is lithium iron phosphate (LFP) with a market share of 30% in 2022. LFP has seen significant growth due to Chinese OEMs, especially BYD, which alone requires up to 50% of the demand (IEA). This is because BYD has made breakthroughs in LFP battery technology with their blade battery, which takes care of two major problems: the reliability of the battery, and the usage of nickel—a rare metal with depleting sources. Innovative solutions such as this indicate the start of a revolution in the automotive industry.

Recharging and Infrastructure

The recharging process is a fundamental drawback of BEVs, as fossil fuel powered vehicles can refuel within a matter of minutes while BEVs may take up to 23,000% more time than standard refueling. Chargers have been divided into 3 levels and these levels are the defining factors for faster charging times. Level 1 chargers are the most basic chargers, with 1 kW of power output and 120V AC voltage; these typically add 2 - 5 miles per hour of charging. Level 2 chargers are the industry standard and the most common ones, and you can usually find these at your home and the nearest charging station, that typically have a power output of 7 - 19 kW with 240V; these chargers add 10 - 20 miles per hour of charging. Level 3 chargers are the fastest chargers and place an immense burden on the grid. Their power output can vary anywhere from 50 - 350 kW and can add anywhere between 180 - 240 miles per hour of charging (US Dept. of Transportation). While level 3 chargers seem like the obvious solution for reduction of charging times, they are extremely expensive to construct and place a huge burden on the power grid, which results in problems with scalability. This also correlates to the "chicken egg problem,"

where the lack of BEVs causes the lack of infrastructure and vice-versa. From Figure 5, it is apparent that the US has made great strides in their infrastructure, with almost 10 times the number of charging stations to gas stations; however, the graph also shows the dire situation in India, which in contrast has more gas stations than charging stations. The foremost reason for increasing the number of charging stations is to become free of range anxiety. Rather than depending on larger batteries, it is better to always have a charging station nearby since larger batteries cost more and require more expensive rare earth metals. Therefore, better infrastructure could solve a variety of problems, especially since chemical composition of a battery is no longer a bottleneck for faster charging but rather the grid and charging stations with low power output (Carrington).

Energy and efficiency

BEVs now have a better cost per mile which had not been possible up until 2022 (Reuter). The average cost of one kWh of energy can vary between 7.7 - 16.7 cents; the same cost per kWh of energy in fossil fuels when calculated had a cost of 13 cents. The difference between these vehicles originates from their percentage of 'useful energy.' For BEVs this percentage averages around 77%, and for ICE vehicles it can vary anywhere between 10-30% due to specific environmental conditions: terrain, highways and a variety of other such factors. This results in BEVs costing between 10 - 21 cents for each kWh of 'useful energy' depending on the country and location; the same measure for ICE vehicles would average around 61 cents. In layman's terms, this would mean that depending on the car and electricity prices, locally BEVs can travel 3 to 6 times further for the same cost as one would have to pay for the fuel of an ICE vehicle.

Conclusions and Recommendations

We have taken a series of factors into account—price, range, charging times, energy efficiency, and costs— which provide a quantitative comparison between BEVs and ICE vehicles. These factors represent each vehicle and their characteristics, and they also allow us to understand the logic behind the cultural shift from ICE vehicles to BEVs. However, as seen from the data presented, BEVs are still lagging behind and to make up for this they need to improve the overall infrastructure or lose their dependence and reliance on the infrastructure. This can also be done by recharging the battery without a charging station, such as with the help of photovoltaic panels embedded in the body of the car.

The concept of solar cars has been around for a long time; however, due to high cost and low energy generation from solar panels, complete self sustainability is not possible. From a recent study it was found that the number of required grid charging events per year can be reduced from 104 to 34 in The Netherlands. Photovoltaic (PV) charging can reduce CO_2 emissions of BEVs by 18% to 93% as compared with ICE vehicles. This information supports PV-powered BEVs to be impactful with some technological breakthroughs in reduction of cost for their upfront cost and improving energy generation in the PV cells. These vehicles could

revolutionize the industry by reducing the fear of range anxiety and reducing the overall grid charging events (Rodriguez et al.).

Acknowledgement

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Syrian Refugee Women's Access to Menstrual Healthcare By Sai Chavan

Abstract

This literature review prefaces the context and history of Syrian refugee women and their experiences living in Turkey. It also describes the experiences of women in regards to their menstrual and reproductive health, especially the correlation between their economic statuses and access to healthcare services and products.

Introduction

The United Nations has announced the Syrian refugee crisis as the worst humanitarian crisis of the 21st century (Kimhwe et al., 2006). Affecting men, women, and children, the public health epidemic has grown increasingly detrimental to thousands of womens' health in Syria, as well as geographical areas bordering the country. Compared to developed and resource wealthy nations, women's health in developing countries has faced many challenges in the past. These challenges include, but are not limited to, maternal mortality, cervical cancer, and HIV/AIDS (Axa). Due to the poor environment of certain regions, individuals living there may suffer as a result of the limitation in availability of natural resources. For example, there is malnutrition amongst individuals of all ages, poor sanitation, increased poverty levels, war and conflict, and lack of a stable water source (Revise Sociology Article). The price inflation among common household items has also led many refugees to migrate to countries that have cheaper prices for necessities.

Turkey is home to over three million Syrians and is also acknowledged as the world's biggest refugee-hosting country (UNHCR). The Syrian refugee crisis began in March of 2011 when millions of Syrians were forced to flee their homes, due to the aftermath of the Syrian civil war. Syrian refugees fled to adjacent countries like Lebanon, Turkey, and Jordan in hopes of finding safer environments to reside in, along with appropriate health care (Samari 2017). The Syrian government displayed acts of violence on the public which instilled a fear in the individuals who were currently living in that area(Ahmet, 2015). Due to less than ideal circumstances, social vulnerabilities were highlighted; especially regarding the health of young women. These include sexual and gender-based violence, unplanned pregnancies, reduced use of modern contraceptives, and infant morbidity (Col et. al, 2020).

Regarding women's menstrual health in particular, the quality of women's health has suffered a great toll ever since the rise of the Syrian refugee crisis and the war crimes in 2011 (UNHCR). For women of childbearing age (18 to 44 years), there is a lack of hygienic products available to care for the basic needs of one's menstrual cycle or reproductive concerns (Alabriya Net).There has been a reduction in the availability of products, like detergent, soap, napkins, baby diapers, and toilet paper (Reuters). Products such as these are critical to a women's reproductive health since they promote good hygiene and ensure the ability to clean oneself appropriately (Daily Sabha Agencies). Tampons are scarce in Turkey, and are only available in certain grocery stores (The Healthy Journal Article). However, pads are more available to use than tampons. Since pads are one of the only sanitary products available, its price has increased

by 50% over the last 10 years alone($4 per 6 pack in 2010 vs. $0.079 for a pad in 2020), providing a socioeconomic barrier to access on a regular basis [Bianet]. The price of branded hygienic products cost around 50 Turkish lira ($2.65 USD), while they cost around $20 in the U.S (Park 2022).

As a result, many women cannot afford to purchase these products for their health and in return are exposed to increased rates of sexually transmitted diseases, reproductive issues, or other health issues (Ashwin et Al.). Women are more susceptible to STDS or other sexually transmitted health issues when they do not have access to adequate health care. The prices have risen with an inflation rate of 2.36% every year (Topcu, 2022). Given this high inflation rate, women who are less affluent may not necessarily be able to purchase such expensive products. This variable should not even be a factor for hygienic products, especially, since everyone should have open access to them to care for their own body in a safe and appropriate manner.

Prior studies assessing women's menstrual health in this area have explored reproductive health in Turkey, inflation rates of hygienic products, and the Syrian refugee crisis overall. However, no comprehensive literature exists detailing the access or barriers to access menstrual products for this same population. Additionally, there is no literature review that assesses the current status of Syrian refugee women's health in Turkey and introduces strategies and recommendations to improve health among this vulnerable population. The aim of this literature review is to fill this gap by providing a comprehensive review surrounding Syrian refugee womens' health in Turkey during a refugee crisis, as well as centralize known facts about womens' health during the crisis which began as early as March 2011.

The research questions guiding the review of the literature are as follows:
1. What are the barriers to access menstrual hygiene products for Syrian refugee women living in Turkey?
2. How are the injustices they face reflective of modern society?

Methods

Due to the lack of available studies, conducting a systematic review or meta-analysis was not possible. This topic involves reviewing literature across disciplines and has been explored by few. The Google Scholar, JSTOR, and PubMed databases were searched for original articles. For the study, we excluded commentary, editorials, reviews, and guidelines. We focused on articles published between January 2016 and December 2022. We used the following keywords and search strings: "Turkey", "menstrual health", "Syrian", "refugee", "reproductive," AND "women". In addition we searched: (Turkey AND Syria), (Turkey OR Syria), (Syrian AND refugee), (Syrian OR Refugee), (Menstrual health AND Reproductive), (Menstrual health OR Reproductive), (Syrian AND Women), (Syrian OR Women), (Turkey AND Women), (Turkey OR Women), (Syrian AND Menstrual Health), (Syrian OR Menstrual Health), (Turkey AND Reproductive), (Turkey OR Reproductive), (Refugee AND Women), (Refugee OR Women), (Syrian AND Reproductive), (Syrian OR Reproductive), (Menstrual health AND Refugee),

(Menstrual health OR Refugee), (Women AND Reproductive), (Women OR Reproductive), (Refugee AND Reproductive), (Refugee OR Reproductive).

A total of 20 articles were obtained after the first initial search. The abstracts were reviewed by SC. The abstracts and full articles were evaluated by SC and KT and selected all studies meeting the following criteria: 1) after 2010 – pre and post Syrian election or war, 2) the paper specifically discusses the type of maternal health (doctor visits overall, menstrual product use, menstrual product education, menstrual access), 3) assesses women of childbearing age (14 to 40 years old). Along with the methods previously stated, we also used inclusion and exclusion criterias. We made sure to use papers that were published after 2010, in order to gain a better understanding of current data. We believe that if the data is more present, there will be less human error in terms of statistics belonging to that issue. It also demonstrates how this topic may display its roots in today's world or cause problems to occur as well. Furthermore, we made sure to observe that specific ages were included to highlight only females who were experiencing menstruation (fourteen to around forty years old). The original search yielded around twenty papers, but we ended up only using around ten or eleven because we wanted to remain as specific as possible. After the criterion for inclusion and exclusion were applied, a total of 9 articles were utilized for the literature review. These articles are located on a google spreadsheet to organize the papers along with their individual themes.
Results:

Theme #1: Pre and post Syrian election and war:

We first examined the paper, "A Comparative Study of Syrian Refugees in Turkey, Lebanon, and Jordan: Healthcare Access and Delivery" (Saleh et. al 2018). Turkey has a different approach which is morality oriented instead of security centered approach towards Syrians refugees (Ara 2015) & Mencutek, . The country has adopted an unconditional 'open door policy'. A policy was adopted by Turkey to grant the right to the Syrian refugees a temporary protection status which gives the temporary asylum. The regulation provides a legal status giving some social rights such as identity card, social support and full access to medical care. Despite the refugee crisis requiring international responsibility, Turkey carried the lion share of such crises and implemented policies beyond hospitality as it was the past. Turkey carries the high expenses of refugee care, including the enormous medical expenses, with minimal support from other countries. Such policies include housing, employment, education and health (personal and public health) (Kirişci, 2014) 460 OPUS Uluslararaswe Toplum Araştırmaları Dergisi.

Next, "Comparison of pregnant Turkish women and Syrian refugees: Does living as a refugee have an unfavorable effect on pregnancy outcomes?" (Turkay et. al 2020) discusses the perspective of being a refugee regarding this particular instance. Being a refugee is usually caused by war, and therefore, is perfect for this category. This study was conducted to determine refugee women's attitudes towards family planning and related factors.According to the study results, Syrian refugees have a higher rate of adolescent birth and low-birth-weight neonates which could

be attributed to poor care and insufficient nutrition during pregnancy while living as a refugee in Turkey.

Theme #2: Types of menstrual health visits:

For menstrual health visits we included doctor visits overall, menstrual product use, menstrual product education, menstrual access. "Syrian Refugee Women's Health in Lebanon, Turkey, and Jordan and Recommendations for Improved Practice" discusses that women's reproductive health should be seen as fundamental to the long term response to the crisis in Syria. Continued efforts towards the MISP objectives, reducing barriers to accessing care, better data collection and evaluation, and improvements in funding and coordination across sectors can improve women's health. If women's reproductive health needs are not met, women are limited in their ability to contribute to social, economic, and political life.

"Knowledge, Attitudes And Practices Of Syrian Refugee Mothers Towards Sexually Transmitted Infections" is another example since it narrows in on sexually transmitted diseases. It states that Syrian refugee mothers have poor knowledge about non-HIV causes of STIs and clinical symptoms. They have poor practices concerning STI screening and prevention. It is imperative that nurses address these issues especially among refugees in locales where resources are scarce.

Theme#3: Adolescents vs. Women of Childbearing Age

"A community-based survey on Syrian refugee women's health and its predictors in Şanliurfa, Turkey" summarizes that the Arabic version of the General Health Questionnaire 12 (GHQ/12) was used for screening for mental symptoms. The 12-Item General Health Questionnaire (GHQ-12) consists of 12 items, each one assessing the severity of a mental problem over the past few weeks using a 4-point Likert-type scale (from 0 to 3). The score was used to generate a total score ranging from 0 to 36. The positive items were rated from 0 (always) to 3 (never) and the negative ones from 3 (always) to 0 (never). High scores indicated worse health (Goldberg and Williams 1988). The Arabic versions of the GHQ-12 are valid psychiatric screening instruments (sensitivity of 0.83 and specificity 0.80).

"Türkiye: UNFPA - Menstrual Hygiene Management among Refugee Women and Girls in Türkiye - September 2022 [EN/TR]" is yet another example of this theme. IIt touches on the fact that refugee women and girls have limited access to information on menstruation; Disposable sanitary pads, followed by homemade cloth are the most used menstrual materials. The research paper, "The attitudes of refugee women in Turkey towards family planning," explains that it was determined that the attitudes of women towards family planning were at the medium level, nearly half of them used a kind of family planning and received its training, and that their attitudes towards family planning were affected by their and their husband's educational level, their income level, the availability of social security, the type of family planning, the utilization of family planning, and spousal support. Based on our study findings, refugee women and their

partners/husbands should be informed on FP and their attitudes towards and the barriers against FP should be investigated by further studies.

Discussion

The present literature review focused on the barriers to accessing menstrual hygiene products for Syrian refugees living in Turkey. The review identified three distinct themes: pre and post Syrian election and war, types of menstrual health visits, and adolescents vs. women of childbearing age. These themes assisted in organizing the available literature and provide insights into the challenges faced by Syrian refugees in accessing adequate menstrual hygiene products and related services.

In the first theme, the review highlighted the unique approach adopted by Turkey towards Syrian refugees, which is characterized by a morality-oriented rather than a security centered approach. Turkey implemented an open-door policy and granted temporary protection for refugees, providing them with social rights and access to limited medical care/resources. Despite bearing the burden of the crisis, Turkey faced challenges in obtaining support from other countries, leading to the need for substantial financial resources to provide healthcare and other essential services. This is quite significant since it is being contrasted with the idea of inflation which also presents another issue for these women.

The second theme highlighted various aspects of menstrual health visits. In the text, it was emphasized that women's reproductive health, including menstrual hygiene, should be considered fundamental to the long-term response to the crisis in Syria. Efforts to reduce barriers to accessing care, improve data collection and evaluation, and enhance funding and coordination across sectors were suggested to improve women's health. Additionally, it was found that Syrian refugee women had limited knowledge about sexually transmitted infections and exhibited poor practices concerning screening and prevention. This highlights the importance of addressing STI-related issues and providing education and resources in settings where those resources are scarce.

In the last theme of exploring age, mental health screening using GHQ-12 revealed that Syrian women in Turkey experienced severe mental health symptoms. These findings alone indicate the need for mental health support services to address the psychological well-being of refugee women. Limited access to information on menstruation and the use of disposable sanitary pads or homemade cloth as the most common menstrual materials were also identified. These articles emphasized the importance of providing comprehensive menstrual health education and ensuring access to affordable and sustainable menstrual hygiene products for refugee women and girls. This way, challenges regarding women's menstrual health would be solved if there was an increased awareness to it. This may lead to the implementation of certain policies to bring about further attention to this issue.

Lastly, It is clear to acknowledge that a gap in knowledge is present between the barriers that women face and the perspectives that other people have on this issue. In other words, there is no documented explanation or observation of how males react towards this injustice. There needs to be further research on other geographical areas that refugees may experience the same battles

with their health. We should strive to find sources of information that provide context for similar locations with similar conditions, in order to compare and contrast it.

This review has several limitations. First, the review relied on a limited number of studies, which may not fully represent the entire body of literature on this topic. Additionally, the studies included in the review focused on specific aspects of the issue and may not provide a complete list or comprehensive understanding of all the barriers that exist in accessing menstrual hygiene products for Syrian refugees. Furthermore, the reviewed studies were conducted in a specific context (Turkey) and may not be generalizable to other settings or refugee populations. Further research should aim to address these limitations.

In conclusion, the literature review highlights the barriers faced by Syrian refugees in accessing menstrual hygiene products in Turkey. The findings underscore the importance of addressing the unique needs of refugee women, particularly regarding reproductive health, education, and access to affordable and sustainable sources of menstrual hygiene products. Policymakers, healthcare providers, and humanitarian organizations should work together to develop and implement comprehensive interventions that address these barriers and promote the overall well-being and empowerment of Syrian refugee women. Future research should further explore the topic, considering a broader range of factors and contexts, to inform evidence-based interventions and policies.

We desired to write a paper that addressed these issues, in order to highlight them and bring about more awareness. There is not a prominent research study that addresses these concerns. We hope to appeal to the Syrian refugee population and make their issues feel heard.

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An In Vitro and In Silico Investigation of Diethyl Phthalate's Effect on Human Immune and Gut Cells Via Apoptosis and Necroptosis By Esther Zhou

Abstract

Diethyl phthalate (DEP) is a commonly used phthalate compound with numerous industrial applications, including plastic products and fragrances. Because of its popularity in consumer products and its ability to easily spread through the environment, humans are exposed to DEP regularly either through inhalation, ingestion, or direct contact. Although limited studies and resources have been dedicated to this particular chemical, the existing investigations of diethyl phthalate suggest harmful consequences to humans exposed to it. Links to inflammatory responses, disturbances in the immune system, or even claims of DEP's carcinogenicity have been suggested; however, these hypotheses were mainly based on rat or other animal experimentation. The influence of diethyl phthalate is still inconclusive for humans. Therefore, further research is needed to elucidate the kind of effect diethyl phthalate would have on humans and determine whether that effect is of concern. This paper investigates the effects of diethyl phthalate particularly on the human immune and gut system by the utilization of cell adhesion, MTT, caspase, and ELISA assays. These assays reveal information about inflammation, cell proliferation, apoptosis, and protein expression in the immune (U-937) and colon cells (CCD-18) that are experimented on in this research. The results from this study provide more insight into the indeterminate health implications of diethyl phthalate on humans and can be used for future risk assessments and regulatory measures.

Introduction

1.1 Diethyl Phthalate

1.1 Diethyl Phthalate

Diethyl phthalate (DEP), or C12H14O4, is a synthetic colorless liquid characterized by a faint odor and a bitter taste (PubChem). It is part of the phthalate family, known to be antiandrogenic—a substance counteracting the effects of androgens (Chen and Ge). The National Cancer Institute defines antiandrogens as substances counteracting androgen effects (National Cancer Institute). Diethyl phthalate is produced industrially by the reaction of phthalic anhydride with ethanol in the presence of a concentrated sulfuric acid catalyst, chemically making it a diethyl ester of benzene-1,2-dicarboxylic acid (PubChem). Its primary application lies in imparting flexibility to plastic materials, leading to its widespread usage in toothbrushes, automobile components, tools, toys, and food packaging (PubChem). Another popular application of DEP includes its role in perfumes as a solvent and carrier for fragrance and cosmetic ingredients and/or as an alcohol denaturant (Kassum). While the Federal Hazardous Substance Act (FHSA) recognizes DEP's toxicity due to its potential to induce several illnesses, the United States has consistently witnessed a substantial annual production of DEP, ranging from 20 to 30 million pounds, since 1988 (Carlson and Patton).

1.2 Effects on the Environment

DEP is considered a persistent organic pollutant, capable of accumulating in the environment (PubChem). The usage of DEP products contributes the most to contamination because of the absence of covalent bonds between DEP and consumer products, allowing the chemical to readily volatilize as gas or vapor (Kwun Omang). However, the measured levels of DEP in the environment stay low because of DEP's ability to degrade anaerobically or aerobically (Williams, Satcher, and Shore). In landfills, where a significant portion of DEP-laden items ends up, product degradation occurs, and DEP may leach into the soil or underlying groundwater, contingent upon the organic matter content of the soil (Mohan et al.). However, processes of breaking down diethyl phthalate are commonly observed. If DEP adheres to organic soil particles or water sediments, microorganisms facilitate its breakdown into innocuous byproducts, such as carbon dioxide (ATSDR).

1.3 Effects on Public Health

DEP has adverse effects on individuals exposed through inhalation, ingestion, or physical contact (Sekizawa and Dobson). Humans face the most risks of DEP exposure when in proximity to hazardous waste sites, within manufacturing facilities, or through certain consumer products (Mohan et al.). While exposure to DEP results in only minimal absorption, it undergoes metabolism once within the body, giving rise to various metabolites, some of which can pose a hazard (ATSDR). Still, only marginal amounts of DEP and its breakdown products persist within human tissues, as the rest are excreted primarily through the urine within an approximate span of two days (Carlson and Patton). Known symptoms of exposure to diethyl phthalate can manifest in the form of headaches, dizziness, nausea, numbness, paresthesia, and weakness in the extremities (NJ Health).

1.4 Correlation to Other Diseases

In terms of diseases, DEP has been identified as an endocrine-disrupting chemical, capable of interfering with hormonal balance within the human body after long-term exposure (Wang and Qian). This disruption can result in critical effects on reproductive health, including disturbances in hormone levels, fertility issues, and developmental abnormalities in offspring as shown by multiple animal studies (Weaver et al.). Males are at particular risk of testicular damage (Johnson et al.). Human studies have also shown potential connections to adverse reproductive outcomes, although further research is required to establish definitive conclusions. DEP's carcinogenic potential is unclear, although studies on animals have suggested the likelihood (Sekizawa and Dobson). Further research is necessary to ascertain the extent of the carcinogenic risk in humans (Sekizawa and Dobson; Sharma et al.). Lastly, DEP has been shown to affect the immune system (Wang et al.). According to a study done on giant freshwater prawns through in vitro experiments, the organisms' hemocytes, after exposure to DEP for more than 10 minutes, died via necrosis. The results of the experiment suggest that the prawns' defense mechanisms

were negatively influenced (Sung et al.). However, the effect of DEP on the human immune response is unclear and would need further studies (Wang et al.).

1.5 Limitations of Current Research

Research on the effects of diethyl phthalate (DEP) on human health faces several limitations. Firstly, ethical considerations restrict conducting extensive experiments directly on human subjects, necessitating reliance on animal models and in vitro studies (SCCNFP). While these studies provide valuable insights, species differences, and varying metabolic processes can limit the extrapolation of results to human populations (Williams, Satcher, and Shore). Additionally, the complexity of human exposure to DEP from multiple sources, including air, water, food, and consumer products, makes it challenging to isolate and quantify the specific effects of DEP alone (Hansen et al.). Furthermore, establishing causal relationships between DEP and certain health outcomes can be complicated by confounding factors.

1.6 Hypothesis

Prolonged exposure to diethyl phthalate induces detrimental effects on the human immune and gut system, promoting an environment conducive to developing various diseases.

1.7 Purpose

The primary objective of this study is to investigate the impact of diethyl phthalate (DEP) on the human immune and gut system due to the limited amount of previous research on this topic. Thus, meticulously designed laboratory experiments were executed on U-937 immune/leukemia cells and CCD-44 colon cells, and the effects were observed through cell adhesion assays, caspase assays, and ELISA tests. By testing on human cells, the observed harmful effects on other subjects could be deemed applicable. Conclusions for DEP's effects on humans would be more known and beneficial to assess DEP's usability and harmfulness for future actions.

Results

2.1 Cell Attachment Assay

Diethyl phthalate had significant effects on cell adhesion. A treatment of 0.2 μM DEP increased cell adhesion by 78.50% when compared to the control (Fig. 1B & 1F). Conversely, a high concentration of 200 μM resulted in a 44.75% decrease in cell adhesion (Fig. 1E &1F). A concentration of 2 μM and 20 μM did not significantly affect the cell adhesion in U-937 cells (Fig. 1F).
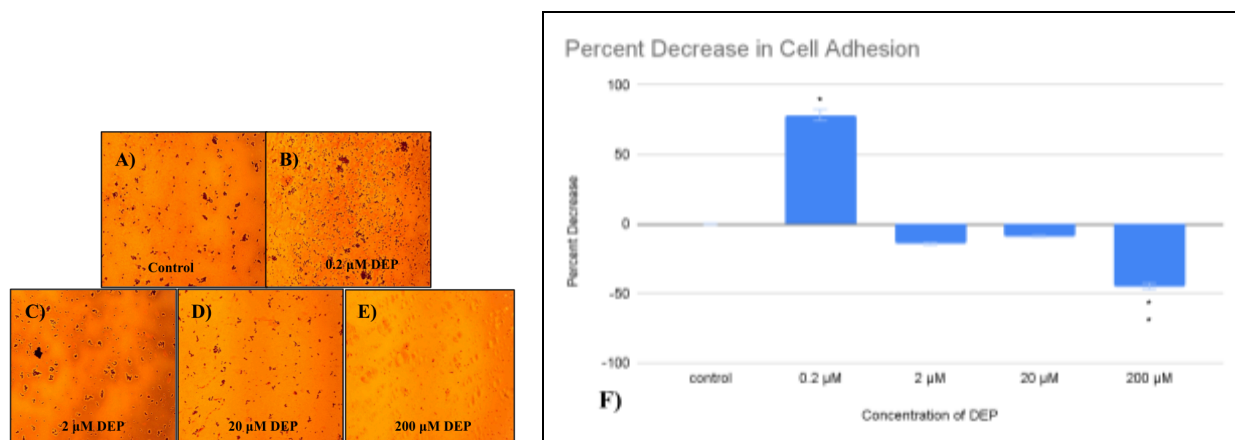
Fig. 1 **Percent Change of U-937 Cells after 24-Hour Exposure to DEP.** A) Control viewed at 40x
magnification. B) DEP 0.2 μM viewed at 40x magnification. C) DEP 2 μM viewed at 40x
magnification.D) DEP 20 μM viewed at 40x magnification. E) DEP 200 μM viewed at 40x
magnification. F) DEP concentrations' effects on cell density**.** Results analyzed using a Bio-rad
microscope. *$p<0.05$, **$p<0.01$, ***$p<0.001$ compared to respective controls. Error bars denote
standard error.

2.2 Decreased U-937 and CCD-18 Cell Proliferation Rate

Diethyl phthalate has significant effects on the viability of U-937 cells. Since a lower
absorbance value correlates to fewer cells, the data from the assay revealed that a high or very low
concentration of diethyl phthalate leads to a decrease in the cell proliferation of U-937 cells after
24 hours (Fig. 2A). There was a 38.68% decrease in the absorbance value when comparing
control cells to those treated with 0.2 μM (Fig. 2A). A bigger percent decrease was seen with the
higher concentrations of 200 μM & 20 μM DEP— 60.38% and 52.63% respectively (Fig. 2A). A
concentration of 2 μM resulted in no significant difference (Fig. 2A).

After 48 hours, the effect of 0.2 μM and 20 μM concentrations was not significant
anymore (Fig. 2B). However, the concentration of 2 μM significantly decreased U-937 cell
survival, resulting in a 47.76% decrease in comparison to the untreated control (Fig. 2B).

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Effect of Diethyl Phthalate on U937 (MTT 48 hrs)

B)
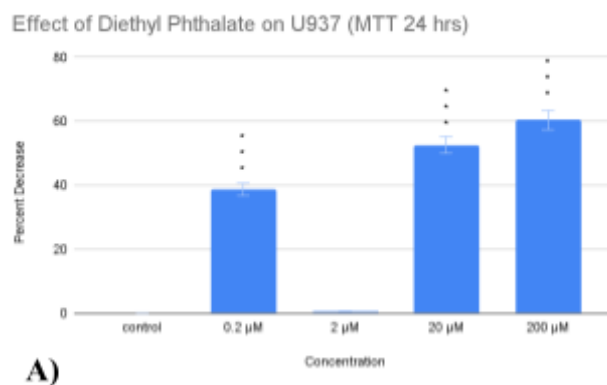
Fig. 2 Percent Change in U-937 Cell Survival After 24 & 48 Hours MTT Assay. A) Effect of Different Concentrations of Diethyl Phthalate on U-937 survival after 24 hours. B) Effect of Different Concentrations of Diethyl Phthalate on U-937 survival after 48 hours. Results colorimetrically analyzed using a Bio-rad iMark microplate reader.
*$p<0.05$, **$p<0.01$, ***$p<0.001$ compared to respective controls. Error bars denote standard error.

      Results for the CCD-18 MTT assay after 24 hours were similar to those of the U-937 assay after 24 hours. The higher concentrations of DEP significantly reduced the cell survival of CDD-18, resulting in a percent decrease of 35.32% for 20 μM and 13.22% for 2 μM. 0.2 μM had no significant change from the control value (Fig. 3A).

      After 48 hours, concentrations of 2 μM, 20 μM, and 200 μM significantly decreased CCD-18 cells even more. 0.2 μM started having a significant impact now with a 19.78% increase when compared to the control (Fig. 3B).

Effect of Diethyl Pthalate on CCD-18 (MTT 24 hrs)

A)

Effect of Diethyl Phthalate on CCD-18 (MTT 48hrs)

B)
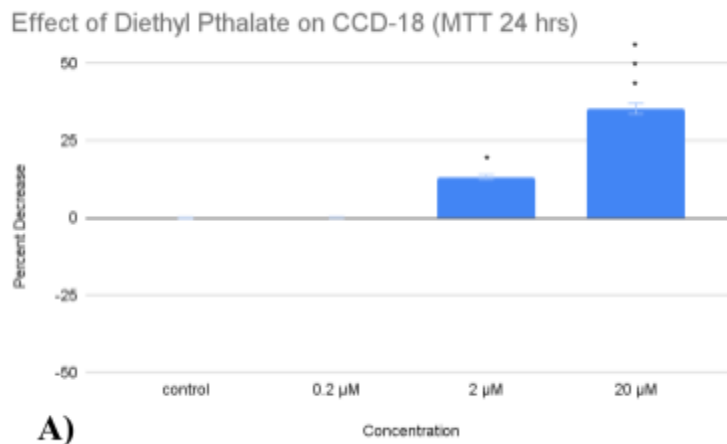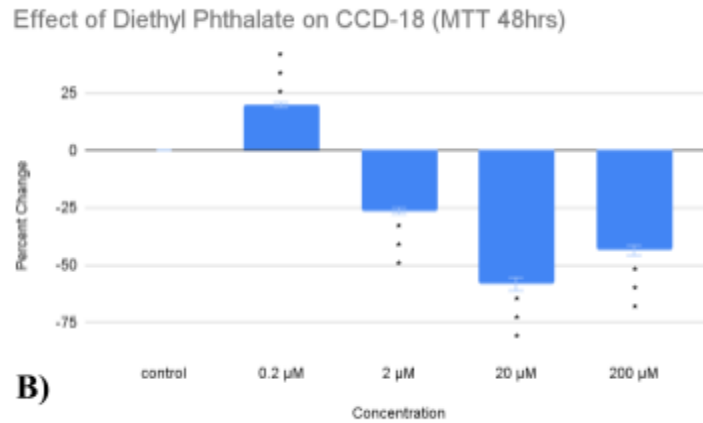
Fig. 3 **Percent Change in U-937 Cell Survival After 24 & 48 Hours MTT Assay.** A) Effect of DEP Different Concentrations on CCD-18 survival after 24 hours. B) Effect of DEP Different Concentrations on CCD-18 survival after 48 hours. Results were colorimetrically analyzed using a Bio-rad iMark microplate reader.
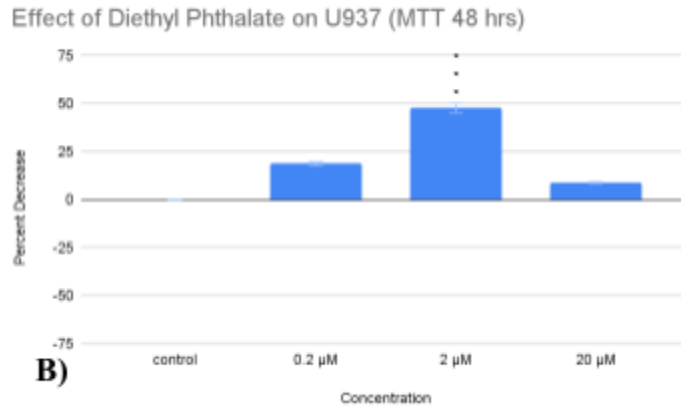*$p<0.05$, **$p<0.01$, ***$p<0.001$ compared to respective controls. Error bars denote standard error.

2.3 MMP-9 Elisa

The MMP-9 Elisa test was performed to analyze diethyl phthalate's effect on MMP-9 expression. The 0.2 µM concentration resulted in a 13.32% decrease in MMP-9 while 2 µM had no significant difference when compared to the control value (Fig. 4).
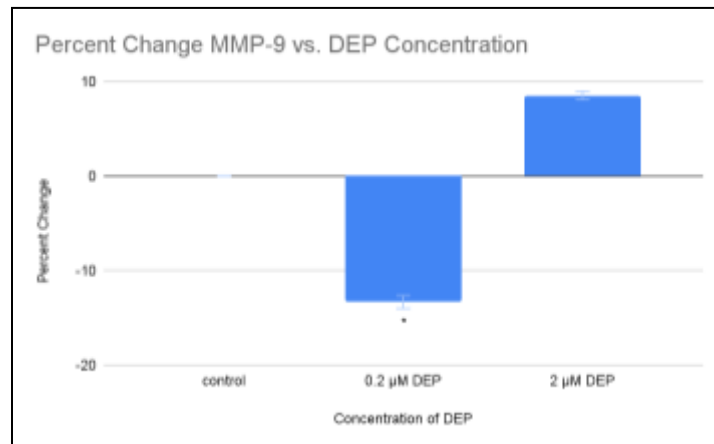
Fig. 4 **Percent Change in MMP-9 Expression After Exposure to DEP.**
*$p<0.05$, **$p<0.01$, ***$p<0.001$ compared to respective controls. Error bars denote standard error.

2.4 BDNF Elisa Data

In all concentrations, diethyl phthalate significantly reduced the amount of BDNF in each well. The higher concentration (2 μM) had a greater percent decrease of 71.70% (Fig. 5). The lower concentration (0.2 μM) had a percent decrease of 64.43% (Fig. 5).
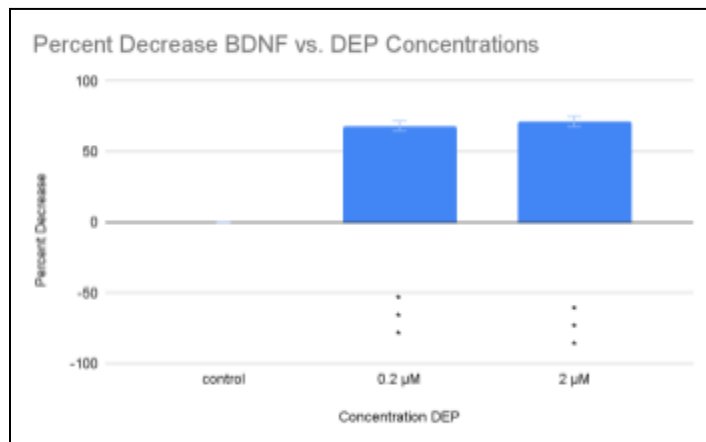
Fig. 5 Percent Change in BDNF Expression After Exposure to DEP.
*p<0.05, **p<0.01, ***p<0.001 compared to respective controls. Error bars denote standard error

2.5 Caspase Results

Diethyl phthalate significantly increased caspase activity in all concentrations which measures cell apoptosis. For a lower concentration of 0.2 μM, caspase-3 expression resulted in a 564.38% increase when compared to the control value (Fig. 6). For a higher concentration of 2 μM, caspase-3 activity had a 387.5% increase (Fig. 6).
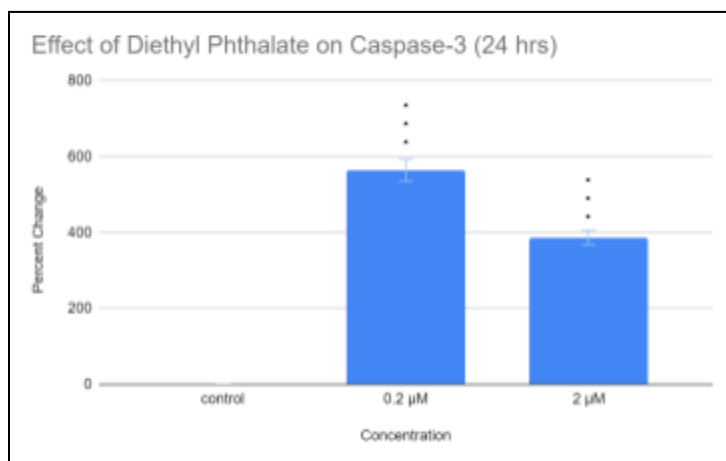
Fig. 6 Percent Change in Caspase Expression After Exposure to DEP.
*p<0.05, **p<0.01, ***p<0.001 compared to respective controls. Error bars denote standard error

2.6 Molecular Docking

Table 1: Binding affinity of different receptors and diethyl phthalate

Receptors	Average Binding Affinity to Dicamba

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CD- 44	-5.8
Receptor-interacting Protein Kinase 1	-5.8
Toll-Like Receptor 6 (TLR)	-5.8
ACE 2 Receptor	-5.5
Tumor Necrosis Factor Receptor 1	-5.4
Matrix Metalloproteinase 9	-5.2
Transforming Growth Factor Beta	-4.8
Interleukin 1 Beta	-4.6
CCKA Receptor	-4.5

Diethyl phthalate had the highest binding affinities with CD-44, RIPK-1, and TLR with a unanimous value of -5.8 (Table 1). DEP has the lowest binding affinity of -4.5 with the CCKA receptor (Table 1).

Discussion

The data from the experiments provide new information regarding diethyl phthalate's (DEP) effects on human immune and gut cells. The first investigation of this lab study employed Cell Image Analysis to quantify the percentage change in cell adhesion between treated and untreated U-937 cells. With information about cell adhesion, links to inflammation can be established, since cell adhesion is activated by an inflammatory response's initiation of reactions through receptor-ligand binding interactions (Fenton et al.), (Chi and Melendez). Based on the results of the study, it can be seen that lower concentrations of DEP enhance inflammation, evidenced by the significant increase in cell attachment observed between control cells and cells treated with 0.2 μM DEP (Fig. 1F). This finding is of importance because 0.2 μM is most similar to the level of DEP found in the environment, meaning humans are exposed regularly to the amount that would induce inflammation (Williams, Satcher, and Shore). Conversely, the imaging results indicated that high concentrations of DEP impede cell adhesion, signified by the decrease in cell adhesion between control cells and cells treated with 200 μM DEP (Fig. 1F). Previous studies have already hinted at the possible association between diethyl phthalate and heightened inflammatory response— this study confirms the association (Smith), (Ferguson, Loch-Caruso, and Meeker).

One possible explanation for the increased cell adhesion is the alteration of integrin-β1 levels. Integrin-β1 is a cell surface receptor that plays a crucial role in mediating cell adhesion to extracellular matrix (ECM) proteins (Trim et al.). When it is upregulated, there are more of these receptors on the cell surface, which allows cells to bind more effectively to ECM components. Recent research has shown that phthalate exposure involves the upregulation of integrin-β1 expressions, so an increase in cell adhesion would be expected (LaFlamme, Akiyama, and Yamada). Furthermore, molecular docking from this research reveals a moderate binding affinity

between diethyl phthalate and TGF-β, which influences the expression and activity of cell adhesion molecules through the regulation of integrins (Shukla et al.). This finding further coincides with the other research.

Secondly, the findings obtained from the U-937 MTT Assay provide indications that diethyl phthalate (DEP) may exhibit anti-carcinogenic properties. Previous investigations have failed to establish a definitive association between diethyl phthalate and cancer (Nishimura), (C. S. PhD). A significant reduction in cell viability was observed after a 24-hour exposure to concentrations of DEP at 0.2μM, 20 μM, and 200 μM (Fig. 2). These findings strongly suggest that diethyl phthalate negatively modulates the proliferation rate of U-937 cells, particularly at extremely high and low concentrations. An intermediate concentration of 2 μM appeared to exert negligible effects on cell viability during the first 24-hour incubation period, but after reaching 48 hours, it also induced a substantial decrease in cell survival. This finding suggests that only long-term exposure to this concentration would allow for its effect. The higher concentrations no longer significantly decreased cell survival after 24 hours, potentially indicating that the treatments had already eradicated the majority of cells.

Because of DEP's ability to decrease the cell viability of U-937 cells, it is suggested that diethyl phthalate could potentially regulate the carcinogenic effects of U-937 leukemia cells. However, the extent to which DEP can be employed as a viable treatment remains relatively uncharted, as there could be dangerous side effects, necessitating further comprehensive investigation to confirm and utilize this finding. Nonetheless, the data strongly implies a profound— and novel— cytotoxic effect of DEP on U-937 cells, underscoring the therapeutic potential of diethyl phthalate to this specific cell line.

U-937 cells also can differentiate into immune cells, including monocytes, macrophages, or dendritic cells in response to different stimuli (Chanput, Peters, and Wichers). As a result, DEP's cytotoxic effect is not only limited to the carcinogenic aspect of the cell line but could also extend to the immune aspect. A separate in vitro study has already demonstrated that phthalates can influence both the innate (monocytes/macrophages) and adaptive (T cells) immune responses (Ferguson, Loch-Caruso, and Meeker). Therefore, the data from this study coincides with what has been previously found; there is now more evidence to support it.

As for the CCD-18 MTT assay, diethyl phthalate detrimentally impacts CCD-18 survival. Higher concentrations of DEP (2 and 20 μM) exhibited a significant decrease in cell viability, but the lower concentration of 0.2 μM did not elicit a significant effect. After a 48-hour incubation period, the higher concentrations continued to significantly diminish CCD-18 cell survival, suggesting that longer exposure leads to more severe effects. On the contrary, the 0.2 μM concentration unexpectedly caused an increase in CCD-18 cell survival (Fig. 3).

Given that CCD-18 cells are derived from colon tissue, the observed impact of DEP extends to colon cells and therefore the gastrointestinal system. The decrease in cell survival with high concentrations of DEP can be possibly explained by phthalates' abilities to substantiate colon cancer cells, as found in previous research (Gopalakrishnan et al.). Investigations into other members of the phthalate family unveiled their potential to induce gut inflammation or alterations

in the gut microbiome, but previous studies did not specifically explore the effects of DEP on colon cells (Chen et al), (Chiu et al.). However, it was predicted that DEP would engender the same effect if similar experiments were conducted. This study not only corroborates the negative impact of DEP on the gut system through significant reductions in colon cell survival but also reveals the novel finding that low concentrations of DEP could potentially yield beneficial effects, such as substantiating CCD-18 cells. The latter claim would need further research and evidence for confirmation.

Regarding MMP-9, studies have explored the effects of other phthalates, such as DEHP, on it, but no conclusion regarding diethyl phthalate's impact was established (Yang et al.). The present study provides evidence that DEP exhibits similar effects to its phthalate counterparts. However, a longer incubation period would need to be employed to draw more definitive conclusions because, in the 24-hour timeframe, the results from 2 μM remained comparable to the ones of the control. As for the significant reduction of MMP9 at the lowest concentration of DEP, it can be implied that DEP could yield additional benefits on top of increasing CCD-18 cell proliferation. MMP9 serves as a marker for various pathological conditions, including cancer metastasis, so a reduction from the 0.2 μM DEP treatment further supports the chemical's potential benefits (Shih, Pan, and Jong Yuh Cherng). Regarding BDNF, DEP at 0.2 μM and 2 μM significantly reduced it. From past in vivo studies, BDNF expression was found to be significantly reduced by inflammation, and as found earlier in cell imaging, 0.2 μM, and 2 μM were suggested to induce inflammation (Cui and Khalil). The data is consistent.

Results from the caspase assay illustrate that diethyl phthalate likely does cause cell death through apoptosis since caspase is an enzyme that initiates apoptosis when activated (Head). There was a significant increase in caspase activity in all concentrations compared to the control. This finding is consistent with previous research, showing an increased level of apoptosis in response to DEP exposure (Eskandari and Eaves),(Warner et al.). Furthermore, because caspase-3 can cause inflammation, it may play some role in the alterations of cell adhesion levels as seen from Cell Imaging (Sun et al.).

From the molecular docking, diethyl phthalate had a decent binding affinity with CD-44, which is a cell surface adhesion receptor that is highly expressed in many cancers (Loppnow, Guzik, & Pryjma). The binding affinity makes sense as diethyl phthalate had significant interactions with U-937, which contains CD-44 as a primary HA receptor (Senbanjo & Chellaiah). Similarly, diethyl phthalate had the same high binding affinity of -5.8 with RIPK-1, which also makes sense since RIPK-1 is a key mediator of inflammation (Mifflin, Ofengeim, & Yuan). Diethyl phthalate's induction of inflammation was already strongly suggested by this study. However, RIPK-1 is also a key mediator of cell death through necroptosis, so molecular docking suggests that cells that do not die via apoptosis most likely die through necroptosis. Lastly, diethyl phthalate had the same high binding affinity with TLR, which is involved with pathogen recognition and activation of innate immunity (Sameer & Nissar). Diethyl phthalate is known to be damaging to immune cells or cause inflammation, so the data is consistent with what was found earlier.

Materials and Methods

      3.1 Solution Preparation

      100 μL of diethyl phthalate (Santa Cruz Biotechnology, USA) was transferred into an empty 1.5 mL tube, which was then filled with 900 μL of Gibco Minimum Essential Medium (MEM). After the solution was serially diluted (x1, x10, x100, and x1000), 5 μL of it was added to either 96-well plates or six-well plates to make concentrations of 0.2 μM, 2 μM, 20 μM, and 200 μM.

      3.2 Cell Culture

      The U-937 (ATCC, USA) human leukemia cell line was isolated from the histiocytic lymphoma of a 37-year-old male (Chanput, Peters, and Wichers, 2015). On the other hand, CCD-18 cells are a human fibroblast cell line derived from the normal colon tissue of a Black, two-and-a-half-month-old, female patient (ATCC). In separate flasks, these cells were cultured at the bottom with Gibco Minimum Essential Media (Thermo Fisher Scientific, USA) supplemented with 10% fetal bovine serum (Invitrogen, USA). The flasks were then placed in an incubator (Thermo Scientific, USA) set at a temperature of 37°C, 5% carbon dioxide, and 95% air for 48 hours. Subsequently, the cells were transferred into a 15 mL tube and centrifuged at 3400 rpm for 4 minutes to form a cell pellet. The old media was then discarded, and 12 mL of fresh media was added to the tube, followed by thorough mixing. This process was repeated multiple times to obtain a sufficient number of cells for the completion of the assays.

3.3 Cell Image Analysis Using U-937 Cells

      Cell image analysis was employed to observe diethyl phthalate's effects on cell number. The U-937 cells from the cell culture were transferred into a 24-well plate that was prepared with 3 μg of collagen IV. The plate was then incubated for 2 hours to create a collagen layer at the bottom. Afterward, 500 μL of media with U-937 cells were placed in each well. Then, 10 μL of the desired DEP treatment was added to 10 wells to create 5 different treatment concentrations with two wells each (200 μM, 20 μM, 2 μM, and 0.2 μM) and two wells for control. The well plate was then incubated for 24 hours. The media was removed after and 400 μL Hema 3 Fixative (Thermo Fisher Scientific, USA) was added to each well to remove water from the cells. After two minutes, the fixative was removed and replaced with 300 μL of Hema 3 Stain (Thermo Fisher Scientific, USA) to stain the cells. After 2 minutes and the removal of the stain, each well was rinsed twice with 1000 μL of distilled water.

      The cells were then observed under a compound microscope at 4x magnification with 4 pictures of each well being taken. All images were quantified through the use of ImageJ for cellular numbers (Rasband, W. S.). Cell image analysis conducted on untreated cells served as the control group while cells treated with the different concentrations of diethyl phthalate served as the experimental group.

3.4 U-937 and CCD-18 Cell Proliferation Assay

The Cell Proliferation Assay was conducted to understand diethyl phthalate's impact on the survival of U-937 and CCD-18 cells with the utilization of MTT (3-(4, 5-dimethylthiazol-2)-2, 5-diphenyltetrazolium bromide) which is converted from a yellow tetrazolium into a purple formazan by the mitochondrial dehydrogenases of viable cells (Sigma Aldrich).

The MTT cell viability assay protocol was performed in 96 well-plates according to ATCC for both U-937 and CCD-18 cells with an exception: 70 μL of detergent reagent (Dimethyl sulfoxide) was added instead of the recommended 100 μL. Row 1 and 6 of the U-937 well plate served as controls with no DEP treatment. Rows 2, 3, 4, and 5 received 5 μL of diethyl phthalate in concentrations of 0.2 μM, 2 μM, 20 μM, and 200 μM respectively. Row 1 served as the control with no DEP in the CCD-18 well plate. Row 2, 3, and 4 were treated with 5 μL of DEP in concentrations of 0.2 μM, 2 μM, and 20 μM respectively. The procedure was repeated again for both U-937 and CCD-18 cells, except the incubation period was longer. The same steps were followed until the first 24-hour incubation period, and then each plate received 5 μL of DEP concentrations again (no MTT yet). The cells were then incubated for another 24 hours. 10 μL of MTT was added into each plate and then the same ATCC protocol was employed from there.

The following formula was utilized to calculate the percent decrease in cell survival when comparing control cells to treated cells.: 100*((control cell survival-sample cell survival)/(control cell survival)).

3.5 MMP-9 and BDNF ELISA Test

A series of Elisa tests were performed on CCD-18 cells following the assay protocol provided by the Boster Bio kit. The first procedure utilized the protein Matrix Metallopeptidase 9 (MMP-9), which serves as an essential marker for physiological processes such as inflammation, while the subsequent round involved the application of Brain-derived neurotrophic factor (BDNF), which functions as a modulator of neurotransmitters and neuronal survival and growth (N. Cui and R. Khali),(S. Bathina and U. N. Das).

3.6 Caspase Assay

Caspase 3 is a cysteine-aspartic acid protease involved in cell apoptosis ((E. Eskandari and C. J. Eaves). The Caspase-3 Assay (Enzo Biochem, USA) was used to determine whether diethyl phthalate can destroy cells by inducing apoptosis (G-Biosciences). In this assay, caspase activity will be determined by an IMark microplate reader which will read the absorbance values of each plate.

2000 μL of media with CCD-18 cells were plated onto a six-well plate and treated with 10 μL of diethyl phthalate (control, 0.2 μM, and 2 μM). The cells were then incubated for 24 hours. After the time was up, the medium was removed and 500 μL of trypsin was added. A timer was set for 3 minutes and then 500 μL of MEM was added and the medium was transferred into 1.5 mL tubes. The tubes were centrifuged for 3 minutes and then the medium was removed, leaving only the cell pellet at the bottom of the tube. 50 μL of lysis buffer was added into each tube and the tubes were vortexed. Then, on a 96-well plate, 50 μL of assay buffer was added to each well, followed by 45 μL of lysis buffer. Then, 5 μL was transferred from the tubes

containing the lysis buffer and the cells into the wells along with 5 μL of caspase substrate solution. The 96-well plate was put into a microplate reader (iMark, USA) and read at 415 nanometers at 0 minutes, 15 minutes, 30 minutes, 45 minutes, and 1 hour.

3.7 Molecular Docking

An in silico test was performed to assess the binding affinity between diethyl phthalate and 9 different receptors through the PyRx v.08 software using the AutoDock Vina option. The macromolecules were taken from publicly available sources (PubChem). Diethyl phthalate was downloaded as a .sdf file from the PubChem Compounds Database. VinaWizard was then utilized to assess for binding affinity.

Afterward, macromolecule and ligand files were imported as a .pdb file into BIOVIA Discovery Studio to generate a 3D structure (Trott, O., & Olson, A. J.).

3.8 Statistical Analysis

All experiments were analyzed for significance through a paired, two-tailed, and student t-test. P-values of less than or equal to 0.05 were considered significant. All error bars represent the standard error of the mean (SEM).

Conclusion

In conclusion, this comprehensive investigation demonstrates that diethyl phthalate (DEP) exerts significant effects on human immune and gut cells, and therefore supports previous research suggesting its induction of inflammation and gut system issues. Furthermore, a novel link to anti-carcinogenicity was made but still necessitates more evidence to confirm this discovery and have DEP considered for potential treatment viability. *In vitro,* diethyl phthalate was able to impede cell adhesion at high concentrations and increase cell adhesion in lower concentrations. In addition, this chemical was able to negatively modulate the proliferation rate in all concentrations of U-937 cells and mostly all concentrations of CCD-18 cells as well (except 0.2 μM). The 0.2 μM reveals the novel finding that a lower concentration of DEP could potentially increase CCD-18 cell survival; however, more evidence would have to be established to support this new claim. Regarding MMP-9 and BDNF, DEP appears to decrease these markers. Additionally, DEP increased caspase activity significantly which suggests that apoptosis is the most prominent cell death pathway. *In silico,* the molecular docking data did not reveal extremely strong binding affinities between any of the receptors tested; however, the strongest affinity was for CD-44 and RIPK-1.

It is important to note that for most of the assays, the cells were incubated for 24 hours after treatment and a longer treatment period could provide different results. Also, for these experiments, the concentrations of DEP tested are not the ones most commonly found in consumer products, except for 0.2 μM. It may be useful to examine the effects of other lower concentrations to model the exposure level humans face daily, which then makes results more applicable. In addition, the molecular docking did not reveal any extreme molecular interactions between diethyl phthalate and the tested receptors, warranting the need for further *in silico* experimentation to discover different molecular interactions that could reveal more effects of DEP on human health.

Overall, this study provides valuable findings that deepen the information available about diethyl phthalate and its actual effects on humans, particularly regarding the immune and gut systems. However, it has also revealed novel ideas such as its anti-carcinogenicity and its ability to increase CCD-18 cell proliferation which can be investigated to extend the knowledge of the effects of DEP on humans even further. This research can be used for a multitude of future studies and especially to reconsider the popular use of DEP in consumer products.

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Assessing the Victorian Government's Solar Panel Rebate to Correct the Positive Externalities of Consumption Associated with Solar Panels By Peter Chen

Abstract

Energy production is the largest contributor to Australia's carbon emissions and solar energy offers a sustainable and renewable solution. Producing solar energy not only reduces consumers' electricity bills, but by replacing energy produced from fossil fuels, solar panels also reduce the amount of greenhouse gases emitted into the atmosphere. This review uses quantitative data to estimate the marginal private benefits and marginal social benefits of consuming solar panels, thereby investigating the extent the Victorian Government's solar panel (PV) rebate to Victorian owner-occupier households increases the marginal private benefits to correct the related positive externalities of consumption.

Introduction

Fossil fuels are the largest contributor to global climate change, accounting for over 75% of global greenhouse gas (GHG) emissions and nearly 90% of carbon dioxide emissions (United Nations (UN), "Causes and Effects"). Climate change is the single biggest health threat facing humanity. Its visible consequences include prolonged droughts, intensified storms and escalating sea levels (UN, "What Is Climate Change?"). The number of countries pledging to achieve net zero emissions continues to grow (International Energy Agency).

Australia is committed to achieving its GHG emissions reduction targets of 43% below 2005 levels by 2030, and net zero emissions by 2050 (Australian Office of Financial Management). Energy production is the largest contributor to Australia's carbon emissions, contributing 33.6% of national carbon emissions (Commonwealth Scientific and Industrial Research Organisation (CSIRO), "What Are the Sources"). Solar energy offers a sustainable and renewable solution and is currently the cheapest form of electricity generation in history (Evans). Therefore, solar energy plays an important role in reducing GHG emissions and addressing the pressing issue of climate change (Office of Energy Efficiency & Renewable Energy). I found this prospect highly intriguing, as the upcoming generation to which I belong are destined to endure the impacts of climate change.

Photovoltaic (PV) cells convert sunlight into electrical energy. To boost their energy output, they are connected in chains to form modules/panels. These modules/panels can be used individually or connected to form arrays. One or more arrays are then connected to the electrical grid as part of a complete solar PV system (Solar Energy Technologies Office).

The state of Victoria also aims to reduce emissions by 50% below 2005 levels by 2030 and net zero emissions by 2045 (State Government of Victoria). On 19 August 2018, the Victorian Government announced the delivery of 700,000 rebates for solar panel (PV) installation as part of a 10-year scheme to provide financial incentives for homeowners with existing homes, homes under construction and rental properties (Solar Victoria Leadership Team, "Solar Panel (PV) Rebate"). I was eager to explore the measures our state government has undertaken to alleviate this global crisis and its overall effectiveness.

Specifically, I wondered whether our state government was encouraging enough consumption of solar panels in Victorian owner-occupier households. Therefore, I formed my research question: **"To what extent does the Victorian Government's solar panel (PV) rebate to Victorian owner-occupier households correct the related positive externalities of consumption?"**

To evaluate the Victorian Government's response to the positive externalities associated with solar panels for Victorian owner-occupier households, I used *ceteris paribus* to assume all other variables to be constant (Tragakes). Therefore, I disregarded that on a broader scope, this rebate also benefits community housing and different-sized businesses, is part of the Victorian Government's Solar Home Program, and works on top of the Federal scheme (Solar Victoria Leadership Team, "Ensuring More Victorian").

In my methodology, I outlined how this externality could be measured, and then used calculations to quantitatively determine the value of the externality to understand the incentive for the Victorian Government's PV rebate. Subsequently, I used quantitative data to calculate the value of the rebate to examine and analyse its results. This instigated an enquiry on the Victorian Government's PV rebate in general and its effectiveness in addressing the positive externalities associated with solar panels.

Methodology for Measuring Positive Externality of Consumption

Solar panels are merit goods, meaning they create positive externalities to society when consumed – where the consumption of solar panels generates positive side-effects that are beneficial to society, which is not involved in the transaction (Tragakes). Whilst individuals benefit from the free energy generated from solar panels, it also helps to mitigate climate change, and the broader population benefits by inhaling cleaner air (Regulatory Impact Solutions). Hence, the Victorian Government may reduce its expenditure on emissions mitigation. To measure a positive externality using economic theory, economists use equilibrium models to determine the externality as a welfare loss.

It is generally considered difficult to measure an externality in practice, as the marginal private and social benefit (MPB/MSB) curves of an externality are typically not closely analysed since there may be complex statistical issues. Economists often use quantitative methods to measure externalities, which entail determining the potential cost of damage to evaluate the expense needed to rectify the externality.

In this case, the externality is considered to be the cost to society when solar panels are under-consumed. Insufficient solar panel installations mean a lack of renewable energy usage, subsequently giving rise to many problems such as poorer air quality. Consequently, there is a significant potential cost when solar panels are not consumed by society. As a result, the externality entails the potential reduction in GHG emissions after the Victorian Government's PV rebate incentivises more Victorian owner-occupier households to install solar panels.

Solar panels have an expected lifespan of 45 years (The Renewable Energy Hub UK). Of the Victorian households with solar panels, the average has a 6 kilowatt (kW) solar system

(Wrigley), and each kilowatt solar system is expected to generate about 4 kilowatt hours (kWh) of electricity per day (Barnes). Therefore, a 6kW solar system will generate about 24kWh/day (8760kWh/year).

To calculate the externality when the solar system is consumed, an equation from the Australian National Greenhouse Accounts Factors (as shown below) was used to estimate how much emissions are physically produced by the burning of fossil fuels at the power

station (Scope 2) and the amount of power and emissions lost throughout the grid network (Scope 3) to generate and transfer the same amount of electricity that a 6kW solar system

State, Territory or grid description	Scope 2 Emission Factors		Scope 3 Emission Factors	
	kg CO₂-e/kWh	kg CO₂-e/GJ	kg CO₂-e/kWh	kg CO₂-e/GJ
New South Wales and Australian Capital Territory	0.73	202	0.06	15
Victoria	0.85	238	0.07	20
Queensland	0.73	202	0.15	41

generates annually. The emissions are expressed on a carbon dioxide equivalent (CO2-e) basis – a metric used to compare the emissions from various GHGs (Eurostat) – using the Global Warming Potential weighting factors (Department of Climate Change, Energy, the Environment and Water (DCCEEW), "Australian National Greenhouse Accounts Factors").

Fig 2.1: Indirect (Scope 2 and Scope 3) emissions from the consumption of purchased electricity from the grid

The following formula was used for estimating Scope 2 and Scope 3 emissions released from electricity purchased through the electricity grid and consumed:

$$t\,CO_{2-e} = \frac{Q \times (EF2 + EF3)}{1000}$$

Where:
t CO₂-e is the emissions measured in CO_{2-e} tonnes.
Q is the quantity of electricity purchased from the electricity grid during the years and consumed from the operation of the facility measured in kWh.
EF2 is the scope 2 emission factor, in kilograms of CO_{2-e} emissions per kWh, as per Table 1.
EF3 is the scope 3 emission factor, in kilograms of CO_{2-e} emissions per kWh, as per Table 1.

Subbing the corresponding values into the equation, it was found that:

$$t\,CO_{2-e} = \frac{8760 \times (0.85 + 0.07)}{1000}$$

$$t\,CO_{2-e} = 8.0592$$

The cost for the Victorian Government to mitigate carbon emissions was essential to show the emissions as a monetary value. However, because Victoria currently does not have a state carbon-pricing system, the cost will be measured through Australian Carbon Credit Units (ACCUs), where each ACCU represents one $t\,CO_{2-e}$ stored or avoided. Given ACCUs cost around 30 AUD ($) each (Clean Energy Regulator (CER), "Australian Carbon Credit Units (ACCUs)"), the cost for the Victorian Government to mitigate the relative emissions of purchased electricity from the grid equivalent to that generated by a 6kW solar system across its lifespan is estimated to be:

$$8.0592 \times \$30 \times 45$$

$$= \$10,879.92 \text{ per household system's lifespan}$$

Because there is currently no published data on the number of households in Victoria in 2023, the most recent census data from 2021 has been used. The 2021 Census counted 2.5 million dwellings across Victoria, where 73.4% of households lived in separate houses (1,835,000) (Australian Bureau of Statistics (ABS), "Snapshot of Victoria"). As of 28 February 2023, 668,246 households have installed a solar system in Victoria (CER, "Postcode Data"). Assuming all dwellings are eligible for the PV rebate, have enough space to install a solar system, the number of 'additional' households that can install a solar system and alleviate the externality is estimated to be:

$$1,835,000 - 668,246$$

$$= 1,166,754 \text{ households}$$

Given a 6kW solar system across its lifespan saves the Victorian Government $10,879.92 on emissions mitigation, the estimated externality is:

$$1,166,754 \times \$10,879.92$$

$$= \$12,694,190,179.68$$

It is worth acknowledging this is a highly rough approximation, especially since the calculation involved the number of households in Victoria in 2021 instead of 2023. Within the timeframe, there has likely been a noticeable change in the number of households. Nevertheless, because this data is from the most recent census and there has been no published work demonstrating solar system consumption decreasing the total economic cost of emissions

mitigation for the Victorian Government, the potentially reduced total economic burden of solar systems can be estimated to be approximately $12.7 billion in 2023.

Thus, the positive externality of consumption can now be demonstrated on a theoretical level, as per *Figure 2.2*.

Figure 2.2 illustrates the free market for solar panels in Victoria, where the marginal social benefits of consumption outstrip the private benefits. Thus, there is an under-consumption of solar panels (Qso→Qe) by approximately 1.2 million households. The difference between the MSB curve and the MPB curve results in this welfare loss, depicted by the purple triangle.

3.0   Victorian Government's Response to Externality

Due to such a significant externality, the Victorian Government has delivered PV rebates to incentivise more Victorian owner-occupier households to consume solar panels. Subsequently, reducing emissions produced from electricity generation, thereby addressing the market failure – where solar panels are under-consumed from the socially most desirable point of view (Tragakes).

Victorian households are eligible to receive a PV rebate if they are the owner-occupiers of the property and their combined household taxable income is below $180,000 per year. Additionally, the property is an existing property valued under $3 million without an existing solar PV system (DCCEEW, "Solar PV Panel Rebate"). However, those who installed their system before 1 November 2009 are eligible to replace or expand their existing system (Solar Victoria Leadership Team, "Solar Panel (PV) Rebate"). The Victorian Government's PV rebate is very effective as its criteria encompass the circumstances of 90% of Victorian households (SolarQuotes).

After contacting an authorised solar provider for a quote, the retailer will upload their quote to the Solar Victoria Portal, which starts the online process for their eligibility assessment. Then they need to upload proof of income and a Council Rates Notice to confirm their details. When eligibility is confirmed, the retailer will claim the PV rebate on their behalf and deduct the rebate amount from the total cost of their system. Eligible Victorian households will then pay the outstanding balance directly to the retailer once the system is installed (Solar Victoria Leadership Team, "Solar Panel (PV) Rebate"). The streamlined process facilitates a straightforward claiming process for households, enhancing accessibility to the rebate.

The PV rebates were delivered by Sustainability Victoria (SusVic) from 19 August 2018 to 30 June 2019 (Victorian Auditor-General's Office (VAGO)). From 2018 to 2019, SusVic delivered 34,000 rebates of up to $2,225 plus an interest-free loan equivalent to the rebate value for eligible Victorian owner-occupier households to install a solar system. However, the loan was required to be repaid in four years (Sustainability Victoria (SusVic), *Sustainability Victoria Annual Report*). Due to insufficient data, monthly trends of the rebate influencing the number of solar panel consumptions cannot be described.

From 1 July 2019, the program delivery was transferred to Solar Victoria (SolarVic), a portfolio entity within the Department of Environment, Land, Water and Planning (DELWP). This

time, SolarVic only delivered rebates of up to $1,400 plus an interest-free loan equivalent to the rebate value – still required to be repaid in four years (Solar Victoria Leadership Team, "Solar Panel (PV) Rebate").

Since an average Victorian household has a 6kW solar system costing on average around $5,627 (Wrigley), and the average Victorian earns $1,327.10/week ($69,009.20/year) (Australian Bureau of Statistics, "Average Weekly Earnings"), it can be seen that the purchase of solar panels likely constitutes a great portion of an average Victorian's income. Hence, the demand for solar panels is likely price elastic – relatively high responsiveness of quantity demanded following changes in price (Tragakes). The increase in Victorian owner-occupier households purchasing their first solar system after the delivery of the rebates demonstrates its price elasticity.

Using Microsoft Excel to calculate the number of rebates received from each firm every month from Solar Homes Program reporting (2019-2020), (2021), (2022) revealed that Solar Victoria delivered 180,626 rebates to eligible Victorian owner-occupier households to install a solar system from 2019-2022 (Solar Victoria Leadership Team, "Solar Homes Program Reporting"). However, it is important to note that these data were last reviewed on 25 January 2023, and there is the potential existence of unconfirmed or unrecorded rebates, particularly for recent months.

3.1.0   Results of Victorian Government's Solar PV Rebate

To answer the research question, the Victorian Government's PV rebates' contribution to increasing Victorian owner-occupier households' solar system installations and reducing carbon emissions produced from Victoria's electricity market must be considered – as these factors ultimately determine the extent to which the rebate corrects market failure. The following data were all compiled from government sources and publications to provide an analysable trend and are expected to be generally reliable.

3.1.1   Victorian Owner-Occupier Households' Solar System Installations

Figure 3.1 illustrates the increase in Victorian owner-occupier households' solar system installations over time. It starts from 2001 because 2001 is the earliest available data point.
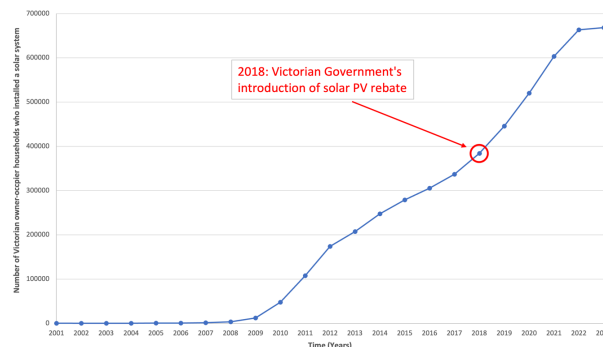
Fig 3.1: Total number of Victorian owner-occupier households who installed a solar system from 2001 to 2023

The Victorian Government's PV rebate had a substantial influence on the annual installation rate, leading to a more pronounced increase compared to the pre-rebate period. This is evident through the steeper gradient observed in 2018, indicating a significant augmentation in installations.

The increased number of Victorian owner-occupier households' solar system installations due to the rebate is equal to the total number of rebates delivered by SusVic (34,000) and Solar Victoria (180,626). Therefore, the Victorian Government's PV rebate has incentivised approximately 214,626 'additional' Victorian owner-occupier households to install their first solar system, who may have otherwise refrained from installing a solar system due to cost constraints. However, it is important to note that this increase in installations may also be due to other factors such as growing awareness of climate change.

As per *Figure 3.1*, from 2018 to 2023, there were 331,276 Victorian owner-occupier households that installed a solar system. 214,626 (≈65%) of them were incentivised by the rebate. This large proportion convincingly suggests the Victorian Government's PV rebate has been largely effective in increasing Victorian owner-occupier households' solar system installations since its introduction. Still, the rebate has only incentivised 214,626 (≈18%) of the 1,166,754 potential 'additional' households that can install a solar system. However, it is important to acknowledge that "the 2022 and 2023 figures will continue to rise" because it takes time for a solar system to be officially recorded and registered, hence the plateau (Clean Energy Regulator, "2021-22 Published Data Highlights").

3.1.2   CO2-e Emissions Produced from Electricity Generation in Victoria

More Victorian owner-occupier households installing solar systems have reduced the dependency on electricity from the grid, of which 71% is produced from fossil fuels (DCCEEW, "Electricity Generation"), thus reducing emissions produced from electricity generation in Victoria. The approximate number of solar systems that have been installed with the rebate (*N*) multiplied by the relative emissions from purchased electricity from the grid equivalent to that generated by a 6kW solar system across its life span (*E*) quantifies the reduction in relative emissions from purchased electricity from the grid.

$$t\, CO_{2-e} = N \times E$$

$$t\, CO_{2-e} = 214,626 \times (8.0592 \times 45)$$

$$t\, CO_{2-e} = 77,837,123.664$$

This value was then multiplied by the ACCU to estimate the cost for the Victorian Government to mitigate the relative emissions from purchased electricity from the grid.

$77,837,123.664 \times \$30$

$= \$2,335,113,709.92$

Therefore, the extent the rebate has corrected the positive externality of consumption can be calculated by dividing this value by the estimated externality:

$$\frac{\$2,335,113,709.92}{\$12,694,190,179.68} \times 100$$

$= 18.395\%$

Whilst this is a relatively small percentage, another way of measuring the effectiveness of the Victorian Government's PV rebate is to calculate its cost-effectiveness. This entails finding the difference between the benefits generated by the rebate (approximately \$2.33 billion) and its implementation costs.

Assuming the Victorian Government granted the maximum rebate value to each of the 214,626 eligible Victorian owner-occupier households, the implementation cost is estimated to be: $(34,000 \times \$2,225) + (180,626 \times \$1400)$

$= \$328,526,400$

Thus, the cost-effectiveness of the rebate is estimated to be:

$\$2,335,113,709.92 - \$328,526,400$

$= \$2,006,587,309.92$

By only spending about \$330 million to incentivise eligible Victorian owner-occupier households to purchase solar panels, the Victorian Government has saved approximately \$2.33 billion on emissions mitigation. Therefore, the Victorian Government's PV rebate is very effective as by incentivising approximately 18% of the total potential additional households, it has yielded emissions mitigation savings exceeding its implementation cost by about \$2 billion.

4.0   Theoretical Effect of Victorian Government's Solar PV Rebate

The impact of the Victorian Government's PV rebate on the market for solar panels in Victoria can be understood on a theoretical level, as illustrated in *Figure 4.1*.

Figure 4.1

Effect of Victorian Government's Solar PV Rebate on the Market for Solar PV Panels in Victoria, Australia

Source: candidate
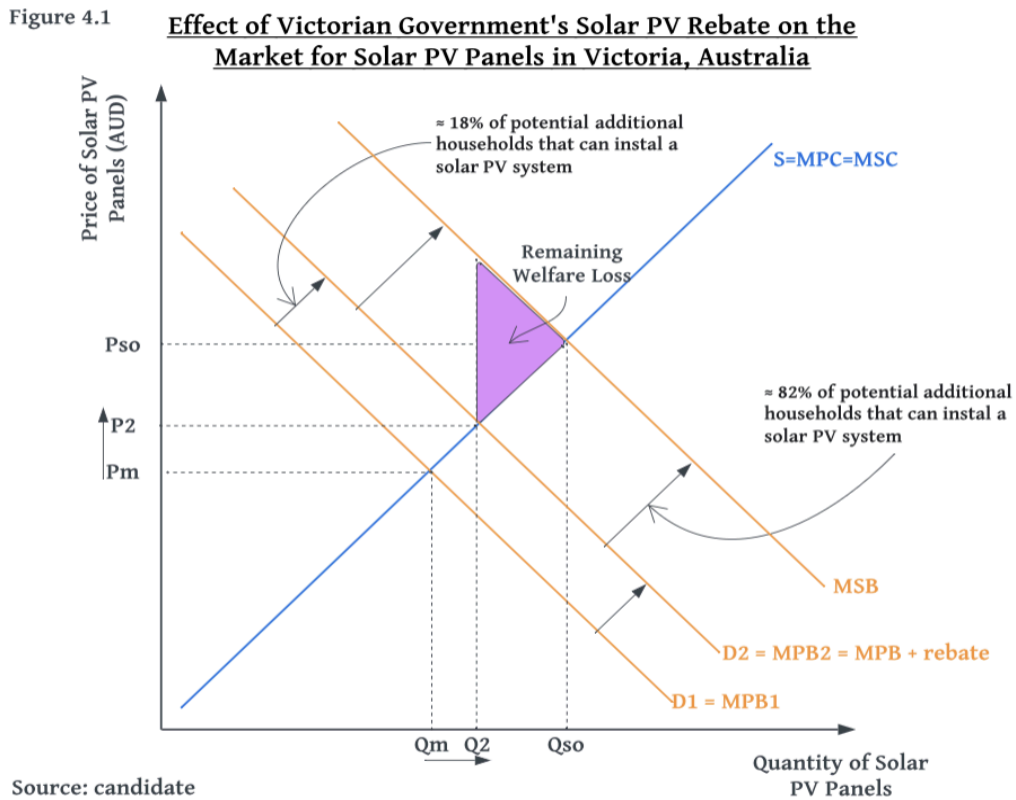
As per *Figure 4.1*, the Victorian Government has increased the demand for solar panels ($D_1 \rightarrow D_2$) through the PV rebate – which has successfully incentivised approximately 18% of potential additional households that install a solar PV system. Consequently, there are more solar panels being produced ($Q_m \rightarrow Q_2$), thereby improving the allocation of resources towards the market for solar panels and reducing the externality's total economic cost by approximately $2.33 billion. Therefore, alleviating the market failure as society nears maximum potential welfare from consuming more solar panels, with fewer emissions in the atmosphere.

However, there is still a potential welfare gain as there remains approximately 82% of potential additional Victorian owner-occupier households without a solar system. Therefore, the Victorian Government could further correct this externality – as reflected by the difference between the new demand curve and the MSB curve.

5.0   Discussion of Victorian Government's Solar PV Rebate

The Victorian Government's PV rebate has successfully incentivised approximately 65% (214,626) of Victorian owner-occupier households' solar system installations since 2018, as discussed in *Section 3.1.1*. Consequently, emissions produced from electricity generation in Victoria have decreased by approximately 78 million $t\ CO_{2-e}$ over the last 5 years. This has improved Victoria's air quality (Regulatory Impact Solutions) and reduced the cost for the

Victorian Government to mitigate emissions by approximately $2.33 billion, thereby reducing approximately 18% of the externality.

Part of why the Victorian Government's PV rebate has successfully incentivised numerous consumers is because solar systems are not only great for society, but they also benefit consumers by decreasing their electricity bills. A typical household in Victoria consumes an average of around 12kWh of electricity per day (Sustainability Victoria). Electricity is charged per kWh, costing on average $0.22/kWh in Victoria (Wrigley). Thus, 12kWh will cost around $2.64/day ($963.60/year) for a typical household in Victoria.

The 6kW solar system generates 12kWh more electricity per day than a typical Victorian household consumes. Thus, Victorians may like to receive feed-in tariffs (FiTs) – the amount one's energy company pays them for the electricity they feed into the grid. The Essential Services Commission sets the minimum that energy retailers must pay for the FiTs, but retailers are free to offer Victorians above this minimum. Retailers can offer solar customers a choice between time-varying or single-rate tariffs (Essential Services Commission).

Under the time-varying FiTs, customers are credited between 5.0 cents and 7.1 cents per kilowatt hour (c/kWh) of electricity exported, depending on the time of day. Whereas the single rate FiTs applies regardless of the time of day and customers are credited 5.2c/kWh (Essential Services Commission). Because time-varying FiTs are subject to numerous variables, such as variations in the timing and quantity of electricity exported by different households, the subsequent calculations will assume that all Victorians chose the single-rate FiTs. To facilitate consistent calculations, the FiTs will be converted to a uniform unit of $0.052/kWh. Based on these assumptions, the estimated amount a typical Victorian household will receive annually from their energy company is estimated to be:

$$[(\$0.052\times12)\times365 \: days]$$

$$= \$227.76$$

The total amount earned annually by a typical Victorian household can be found by adding $963.60/year saved on electricity bills to this value:

$$\$227.76 + \$963.60$$

$$= \$1,191.36$$

This is slightly more than the $1073/year saving for typical households who install solar panels, as projected by the Solar Victoria Leadership Team (Solar Victoria Leadership Team, "Solar Panel (PV) Rebate").

The payback period of a 6kW solar system can also be found by dividing its cost by this value:

$$\frac{\$5,627}{\$1,191.36} \approx 4.72$$

Thus, a 6kW solar system can achieve cost equilibrium within five years, while households will subsequently be annually earning $1,191.36 starting from the fifth year.

Therefore, an average 6kW solar system throughout its lifetime could save a typical Victorian owner-occupier household about $48,000. Many households have likely realised the potential savings and/or wanted to reduce their impact on climate change, hence the growing trend of Victorian owner-occupier households' solar system installations before the rebate, as illustrated in *Figure 3.1*. By reducing the cost eligible Victorian owner-occupier households pay for the solar system, the Victorian Government's PV rebate has further increased the benefits to the consumers. Thus, households were more willing and able to purchase a solar system.

It is important to note, however, that these equations assume the 6kW solar system to be consistently generating electricity like they were brand new, while in reality the solar system's productivity could decrease at a rate of 0.5% per year (Mow). Moreover, it does not consider other factors that may limit the solar system's electricity generation, such as the climate, installation location, and roof spacing. For example, the solar system cannot maximise its solar electricity production in an area with frequent cloudy days or when it is obscured by nearby trees or other structures. Hence, the values calculated above are rough estimations.

Furthermore, when network voltage is not optimal, households are limited in their ability to both self-consume and sell the electricity generated by their PV panels. Thus, they are unlikely to reap the full benefits of installing a solar system and hence are increasingly at risk of not being able to fully understand the benefits of their investment (VAGO).

Fig 5.1: Number of SolarVic's PV rebates received by Victorian owner-occupier households from July 2019 to December 2022

Figure 5.1 portrays a substantial public endorsement of the Victorian Government's PV rebate. The highest-ever annual distribution totalling 62,530 rebates was delivered in 2020. Concurrently, Australia installed its highest-ever number of rooftop solar panels, with the top three instalment postcodes in Victoria (CSIRO, "Australia Installs Record-Breaking Number of Rooftop Solar Panels").

By incentivising more households to purchase solar systems, the rebate helps the state reach its target of reducing emissions by 50% below 2005 levels by 2030. Simultaneously, it increases the derived demand for labour in the solar market, thereby bolstering clean energy jobs (Ore). Every dollar of investment in renewables creates three times more jobs than in the fossil fuel industry (UN, "Causes and Effects"). In April 2021, SolarVic estimated that the program created 4,711 jobs (VAGO).

The downward trajectory observed in *Figure 5.1* may have occurred because more Victorian owner-occupier households have installed a solar system (as shown in *Figure 3.1*), and hence are no longer eligible for another rebate. It may also be because these data were last reviewed on 25 January 2023, and there may still be some unconfirmed or unrecorded rebates, particularly for recent months.

Whilst the Victorian Government's PV rebate has been successful in increasing Victorian owner-occupier households' solar system installations and reducing emissions from electricity generation, there have also been some limitations that come with the rebate. *Figure 4.1* shows
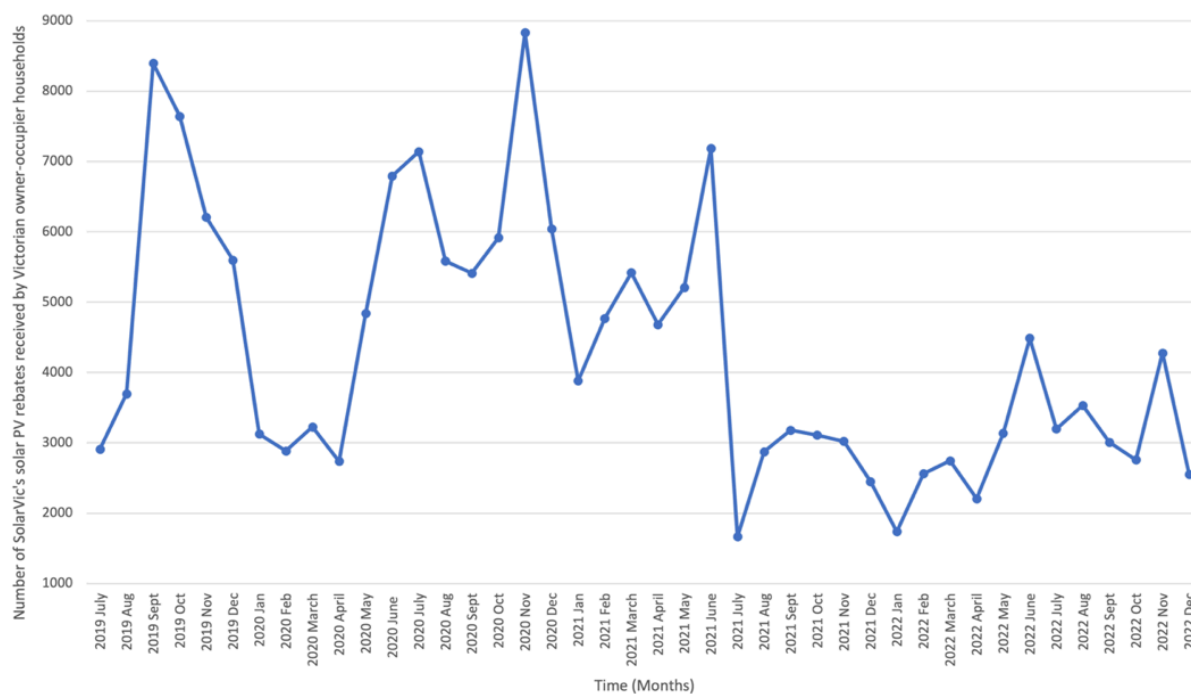
how increased demand (MPB→MPB$_2$) may place upward pressure on prices (P$_m$→P$_2$). Retailers

are likely setting higher prices, as consumers, even after receiving the rebate, are still paying close to the initial price of solar panels before the rebate (VAGO), thus undermining the effectiveness of the rebate in reducing its costs and increasing demand for solar panels.

Moreover, the Victorian Government faces an opportunity cost. Instead of spending government revenue to incentivise Victorian owner-occupier households to install solar systems, they could have funded better public healthcare, education, or even subsidised solar panel producers. The latter would likely reduce producers' costs of production. Thus, they may be more willing and able to increase investment expenditure and conduct further research and development which may increase their productive capacity and hence output. Therefore, the supply of solar panels will increase, placing downward pressure on its price, making it more affordable for consumers and more solar systems may be purchased as a result. Ultimately, this will likely achieve the same goal as the Victorian Government's PV rebate. However, a subsidy may disincentivise producers to produce more efficiently since they are guaranteed payments from the government. Additionally, subsidies generate a deadweight loss, thus reducing overall benefits. Therefore, the PV rebate is the most effective in correcting the market failure.

It is also worth acknowledging that older citizens might be content with their lifestyle and not care as much about making significant improvements to their home, thus less willing to purchase a solar system. Moreover, there could still be people who are unaware of the rebate despite the notices from the government and hence not purchase a solar system. There could also be people who do not acknowledge climate change and consequently choose to not purchase a solar system. Furthermore, there was relatively low economic well-being during COVID-19, with many Victorian households struggling to maintain adequate income levels. Therefore, lower and middle-income households were more likely to save money and purchase only necessary goods and were less willing and able to purchase more expensive goods like solar systems. Potentially in the long term, when Victorian households attain a more adequate and stable income, then they might be more willing and able to purchase a solar system. Additionally, a higher rebate value may also help incentivise more households to purchase a solar system.

Conclusion

From this investigation, it can be stated that **the Victorian Government's solar panel rebate has been very successful in correcting the positive externalities of consumption of solar panels**, seeing it has reduced approximately 78 million $t\ CO_{2-e}$, and will continue to reduce more. However, due to many factors such as Covid-19's impact on Victorians' economic well-being, the rebate only incentivised approximately 18% of potential additional Victorian owner-occupier households to install their first solar system. If the government wishes to correct the externality to a larger extent, it may wish to increase the value of the rebate to incentivise more Victorian owner-occupier households. Nevertheless, this rebate has been very effective as it has saved the Victorian Government around $2 billion more in emissions mitigation than its implementation cost and will contribute to Victoria reaching its target of a 50% reduction in emissions by 2030 (Ore).

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How the Brain understands Music and how Music Therapy is used to treat various mental Illnesses: Autism Spectrum Disorders, Parkinson Disease, Anxiety By Andy Krasulski

Abstract

Music Therapy is bipartite. First is music, which starts as the brain's perception of sound. Frequency, rhythm, pitch, and tone are all critical aspects of music. Once our brain interprets those key parts of the sound, sound transforms into the harmonious melodies we know as music. The second component of Music Therapy treats patients with various mental health issues. By combining both, Music Therapy helps address patients' physical, emotional, cognitive, and social needs. This article provides a framework to visualize how human minds understand sound and music, and the potential that music therapy has shown in treating Autism Spectrum Disorders *(ASD)*, Parkinson Disease *(PD)*, and Generalized Anxiety Disorder *(GAD).*

Auditory Pathway and Processing

This section provides a step-by-step guide on how the brain processes sound, including sound qualities such as rhythm, pitch, and tone. When vocal, instrumental, or mechanical sounds have rhythm, melody, or harmony, the result is music. (*Definition of MUSIC*) The human body receives sound input via vibrations that create sound waves in the air. The primary mechanism that senses these sound waves is the auditory pathway.

This pathway starts in the ear, which consists of the outer, middle, and inner ear. Sound waves enter the outer ear via the external acoustic meatus, a part of the ear that collects sound waves and funnels them into the ear canal (auditory meatus). The sound is amplified and progresses toward the tympanic membrane (eardrum). The eardrum provides a surface for sound collection, and vibrates with frequencies between approximately 20 and 20,000 Hz (Martini and Nath). When the eardrum vibrates, three tiny bones in the ear, the malleus, incus, and stapes, vibrate in unison. These vibrating bones amplify the sound to make sound waves understandable to a human brain. The stapes transfers the vibrations to the oval window (a tissue connecting the middle to the inner ear), transferring the pressure waves to the fluid-filled cavity within the inner ear, which is referred to as the cochlea. The fluid-filled cochlea is encased in bone, so the liquid does not leak. Once pressure is applied at the oval window, the fluid has nowhere to bulge except the other exit, the round window. In other words, the round window bulges outward as the stapes moves inward. As the stapes vibrates at the frequency of the sound arriving at the eardrum, pressure waves travel throughout the cochlea. The pressure waves in the cochlea disturb the basilar membrane, which supports the auditory sensory epithelium, the Organ of Corti. The basilar membrane interacts with the previously mentioned oval window to control frequency. The Organ of Corti is the sensory part of the inner ear. High frequency sounds have a short wavelength, vibrating the basilar membrane near the oval window. Lower frequency sounds have longer wavelengths, vibrating the basilar membrane further from the oval window. The ultimate purpose of this membrane is that frequency is interpreted as information about position along the

basilar membrane (Martini and Nath). This interpretation of frequency translates to understanding different frequencies in music.

Louder sounds move the basilar membrane more. This is because the amount of movement at a given location depends on the magnitude of force applied by the vibrating stapes, which depends on the sound wave's energy. The vibration of the basilar membrane causes vibration of hair cells in the cochlea. These hair cells rest in rows in a structure of the inner ear called the organ of Corti. A soft sound may stimulate only a few hair cells in a portion of one row. As the sound intensity increases, more hair cells become stimulated and active. In short, the number of hair cells responding in the organ of Corti provides information on the intensity of the sound. Vibration of the basilar membrane moves these hair cells against the tectorial membrane, which depolarizes the hair cells. (Martini and Nath). Hair cell depolarization stimulates sensory neurons. The cell bodies of these sensory neurons are located at the center of the cochlea in the spiral ganglion. The spiral ganglion holds sensory neurons and relays information through sound signals from the inner ear to the brainstem. From that point, the data is carried by the cranial nerve VIII cochlear branch to the medulla oblongata cochlear nuclei for distribution to other brain centers. This is where sound starts to be processed as music.

Cranial nerve VIII is the vestibulocochlear nerve and consists of the vestibular and cochlear nerves, which are generally responsible for balance and hearing. This essay's focus is on the cochlear nerve responsible for hearing. More specifically, this nerve is responsible for transmitting auditory signals from the inner ear to the cochlear nuclei within the brainstem and ultimately to the primary auditory cortex within the temporal lobe (Bordoni et al.). To summarize the auditory pathway, auditory sensations are carried by the cranial nerve VIII cochlear branch to the medulla oblongata's cochlear nuclei. From there, the information is relayed to the inferior colliculus, a center that directs various unconscious motor responses to sounds. Ascending acoustic information goes to the medial geniculate nucleus before being forwarded to the auditory cortex of the temporal lobe. The auditory cortex of the temporal lobe is a significant player in pitch. High-frequency sounds activate one portion of the cortex, while low-frequency sounds activate another. The auditory cortex contains a map of the organ of Corti. Thus, information about frequency, translated into information about position on the basilar membrane, is projected in that form onto the auditory cortex, where it is interpreted to produce a person's subjective sensation of pitch (Martini and Nath).

Regarding rhythm, a research report used fMRI to identify brain areas involved in auditory rhythm perception." The following regions responded to rhythm sequences: Dorsal premotor cortex (PMD), SMA (Supplementary motor area: Brain area located in the midline cortex, anterior to the primary motor cortex), preSMA, and lateral cerebellum (Bengtsson et al.). While rhythm is a significant part of music, tone is also a major player. The auditory cortex in part recognizes and understands tone. This part of the brain, along with the cerebellum and prefrontal cortex, also works on analyzing a song's melody and harmony ("Your Brain on Music"). There is so much involved in processing rhythm, pitch, tone, emotion, and memory. However, this is what makes music and the brain such a fascinating combination. With so many

sectors of the brain that music is able to affect, music therapy has the potential to cure so many illnesses.

History of Music Therapy

   Music therapy is an art-based health profession that uses music experiences within a therapeutic relationship to sculpt treatments in order to address MT patients' physical, emotional, cognitive, and social needs (Stegemann et al.). Although music therapy is commonly known to be a recent development, the earliest known reference to music therapy appeared in 1789 in an unsigned article in *Columbian Magazine* titled "Music Physically Considered." During the 1800s, the first recorded systematic experiment in music therapy took place: A neurologist in New York City, James Leonard Corning (1855-1923), used music to alter dream states during psychotherapy. He believed that during pre-sleep and sleep, cognitive processes became dormant, allowing the penetration of "musical vibrations" into the subconscious eliminating morbid thoughts that plagued his patients. (Davis)

   In the 20th century, many more Music Therapy organizations were established. In 1903, Eva Augusta Vescelius founded the National Society of Musical Therapeutics. In 1926, Isa Maud Ilsen founded the National Association for Music in Hospitals. In 1941, Harriet Ayer Seymour created the National Foundation of Music Therapy. However, none of these foundations developed an official clinical profession for Music Therapy that we would see today in something like the clinical profession of Pediatrics. (American Music Therapy Association). In the 1940s, three innovators stood apart. They were the ones to push forward the development of music therapy as an organized clinical profession. Particularly, the "father of music therapy," E. Thayer Gaston, moved the profession forward from an organizational and educational standpoint. The first music therapy college training programs were also created in the 1940s. Michigan State University established the first academic program in music therapy (1944) (American Music Therapy Association).

   More recently, the American Music Therapy Association (AMTA) was formed in 1998, merging the National Association for Music Therapy (NAMT) and the American Association for Music Therapy (AAMT). AMTA is the largest music therapy association in the United States, representing music therapists in the United States and in over 30 countries around the globe (American Music Therapy Association). Although regarded as a recent profession, music therapy has come a long way. Everything branched from James Leonard Corning's psychotherapy to the "father of music therapy," prominent E. Thayer Gaston, and finally to various music therapy college training programs and the respected clinical profession that is seen today.

Music Therapy Today

   There are four main types of music therapy today. Receptive music therapy is a style in which the client listens to music and responds to the experience silently, verbally, or through another manner (eg. art, dance). Receptive interventions are more appropriate when a client is nonverbal or prefers a passive approach through listening. The goal of receptive music therapy is

to improve relaxation, facilitate memory, and develop auditory skills, all whilst enhancing mood and reducing anxiety (Parkinson).

On the contrary, Re-creation is a music-centered approach where the client is encouraged to play or sing along to a pre-composed song to support identified goals. Re-creation can involve singing familiar or new songs or playing various instruments. Re-creation interventions suit children with developmental delays, clients with acquired brain injury, or seniors with Dementia. Goals pertaining to Re-creation music therapy include strengthening motor skills, social interaction, and promoting the use of one side of the body (Parkinson).

Improvisation is arguably the most adaptable, in which this style of music therapy involves spontaneous music-making using simple instruments, body percussion, or the voice. This method requires the therapist to hear, interpret, and respond to the client's playing or mood. Improvisation may be helpful with those who are nonverbal or feel uncomfortable expressing themselves directly. Improvisation music therapy aims to manifest an individual's expression and communication through music, all whilst limiting verbal communication to a comfortable level. This style also focuses on increasing freedom of choice while building a relationship with another individual through music (Parkinson). Lastly, Composition / Songwriting is a creative process whereby the therapist supports the client in creating their own music or lyrics. These creations may be recorded or performed thereafter. Songwriting centers on externalizing emotions, and fostering different manners of expression and creativity. These four types of music therapy can achieve various goals, ranging from promoting relaxation to stimulating creativity (Parkinson). These goals are all general benefits of music therapy that can be achieved while staying non-invasive and lacking side effects. Moreover, music therapy is unique in its ability to address multiple symptoms at once, all while staying cost-effective (Bleibel et al.). For example, receptive music therapy can improve stress and memory at the same time. The idea behind Music therapy is to use music and/or elements of music (like sound, rhythm, and harmony) to accomplish goals, like reducing anxiety or caring for other illnesses such as depression. A patient would first contact their healthcare provider. The healthcare provider would then talk to a music therapist, addressing the patient's needs, music preferences, and experiences. The therapist would then tailor each session specifically to the patient's preferences. They also evaluate the patient's progress throughout these sessions, all whilst working with other healthcare providers to coordinate the patient's care ("What Is Music Therapy, and How Can It Help Me?").

Illnesses Music Therapy Cares for:

Music Therapy is very efficient in its process, but what illnesses does it care for? I will discuss three diseases in this section: Autism Spectrum Disorders (ASDs), Parkinson's, and Anxiety. Autism Spectrum Disorders are a group of neurological disorders characterized by social communication impairments as well as the presence of stereotyped and repetitive behaviors and interests (Bhat and Srinivasan). Music-based therapies form about 12% of all autism interventions

(Bhat and Srinivasan). Other treatments for autism include medication treatment and behavioral management therapy (*What Are the Treatments for Autism?*).

A study was conducted on the effects of signed and spoken words taught with music on sign and speech imitation by children with Autism. The study examined ten 4–9 year-old children with autism, split into two groups. In the study, two sections within Group 1 had music listening ("Goldilocks Returns") condition training in the 1st week and rhythm condition training in the 2nd week. Group 2 had vice versa. There were 5 trials daily, 4 days in two weeks times. The overall results showed that the children had correct imitations (signs, words) and favored music listening over rhythm condition training (Buday). In another study, the aim was to determine the effects of developmental speech and language training through music on verbal production. There were fifty 3–5-year-old children with ASD for the subjects of this study. The study included both music and speech training. The children watched music and speech videos for two times a day for three days via TV Monitor. The outcome showed a major improvement in speech production in children with ASD in both music and speech training. There were also greater improvements shown in low functioning children in the music than in the speech training. (Lim). Children with ASD also proved to have improved understanding of emotion through music therapy. In one study, the objective was to determine effects of background music and song tests on emotional understanding. The test included twelve 9–15 year old children with autism. Background Music was played, the children sang songs, and there were Eight 30 min sessions two times a week Pre and Post Tests. The children also improvised piano pieces based on four emotions; happiness, sadness, anger, fear. The outcomes of the study showed that all children improved significantly in their understanding of these four previously stated emotions. The background music was the more effective part of the study to the children (Katagiri). These studies proved successful in using various music therapy approaches to improve sign and speech as well as comprehension of emotion in children with ASD's.

Music therapy has also shown to be effective in Parkinson's patients."Parkinson's disease (PD) is a neurological disorder involving the progressive degeneration of the dopaminergic system, which gives rise to movement-related dysfunctions (such as bradykinesia, tremor, and rigidity) (Raglio). Music acts as a specific stimulus to obtain motor and emotional responses by combining movement and stimulation of different sensory pathways (Pacchetti et al.). In a 3 month study about active Music Therapy in Parkinson's Disease, thirty-two patients with PD, in two groups of 16 patients each, had weekly sessions of music therapy and physical therapy (PT). The severity of PD was assessed with the Unified Parkinson's Disease Rating Scale, emotional functions with the Happiness Measure, and quality of life using the Parkinson's Disease Quality of Life Questionnaire. Music Therapy sessions consisted of choral singing, voice exercise, rhythmic and free body movements, and active music involving collective invention. PT sessions included a series of passive stretching exercises, specific motor tasks, and strategies to improve balance and gait. Music Therapy had a significant overall effect on bradykinesia as measured by the Unified Parkinson's Disease Rating Scale ($p < .034$) (Pacchetti et al.). Bradykinesia means slowness of movement and speed (or progressive hesitations/halts) as movements are continued.

It is one of the cardinal symptoms of Parkinson's disease (*Bradykinesia (Slowness of Movement) | Parkinson's Foundation*). Post–MT session findings were consistent with motor improvement. ($p < .0001$). Changes on the Happiness Measure confirmed a beneficial effect of MT on emotional functions ($p < .0001$). Improvements in activities of daily living and in quality of life were also documented in the MT group ($p < .0001$). Lastly, PT improved rigidity ($p < .0001$) (Pacchetti et al.). These studies, showing improvements on symptoms like bradykinesia, prove one step at a time that music therapy is a reliable source of treatment for large-scale illnesses in the present world, such as Parkinson's disease.

Anxiety is a feeling of worry, nervousness, or unease, typically about an imminent event or something with an uncertain outcome. In a review of Music Therapy and Other Music-Based Interventions in Pediatric Health Care, the effect of music listening in reducing anxiety was measured in 11 studies. Effect sizes for anxiety reduction ranged between $d = 0.61$ (moderate effect) and $d = 1.5$ (notable effect) (Stegemann et al.). The findings of another study show the effect of music therapy on the anxiety and depression of patients with cancer. Starting levels of depression and anxiety were assessed using the HADS questionnaire 24-hour intervention. Then, patients listened to music for at least 20 min per day for 3 consecutive days, completing the hospital anxiety and depression scale (HADS) questionnaire at the end of each day. The type of music was based on five experts' opinions. The tape was recorded in the form of relaxing light music like the sea, rain, and water sound. The results demonstrated a significant reduction in the mean scores of anxiety and depression in the intervention group. The Control group's mean scores of anxiety and depression went from 14.72 ± 2.06 to 14.34 ± 2.48 by their 3rd day of music therapy. However, the Music Therapy Group (Intervention group)'s mean scores of anxiety and depression plummeted from 14.46 ± 2.13 to 8.63 ± 2.57 by their 3rd day of music therapy (Jasemi et al.). This change in scores corresponds to a reduction in the patients' anxiety and depression. These studies' scores especially highlight music therapy's impact on caring for wide-scale illnesses today.

Conclusion:

Music is sound in its most basic form. It may start as vibrations in the air, but through auditory processing in the inner ear, and the auditory pathway to the brain, music can turn from sound into a source of enjoyment or healing. This simple premise is the basis of Music Therapy. Through the studies shown thus far, MT has proved to help patients with ASD's, PD, and Anxiety. As music therapy is non-invasive and effective, there are still aspects of these illnesses it cannot address on its own. Thus, it should be used most effectively to supplement more intensive treatments. Moreover, MT is used to treat many other illnesses, such as Alzheimer's or Depression, while being used in an experimental state to treat memory loss. This points out that Music Therapy is an effective and rapidly growing healthcare sector today. Further research into memory and emotion will enhance the settings and illnesses to which music therapy can bring its benefits.

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The Advances and Regression of Reproductive Rights in the United States By Sanya Somani

Abstract

       This paper explores the trajectory of reproductive rights in the United States. The pre-1960s marked an era of restriction to contraception with societal taboos. The 1960s marked a significant turning point in American history when birth control was introduced, empowering women to take control of their bodies. However, the post-1960s reveal a regression in reproductive rights with access to contraception and abortion decreasing.

       The legal protections of abortion and reproduction have faced significant challenges with its progressing and regressing. With landmark Supreme Court Cases Griswold v. Connecticut (1965) and Roe v. Wade (1973) recognizing privacy and abortion, America started making progress by empowering females. Yet, recent years have witnessed legal setbacks shown in the 2022 Supreme Court decision in Dobbs v. Jackson's Women's Health Organization, overturning Roe v. Wade and Planned Parenthood v. Casey.

       Public perception of reproductive rights has evolved with society's views shifting from pre-1960s restrictive attitudes to greater acceptance in the 1960s. Nevertheless, recent years reflect a troubling regression marked by anti-abortion laws and the politicization of reproduction. Women of color continue to face disproportionate challenges in access to reproductive healthcare as well. This paper emphasizes the importance of halting this regression to ensure individual autonomy and freedom for women in the United States.

Introduction

       American birth control activist Margaret Sanger once said, "No woman can call herself free who does not own and control her body. No woman can call herself free until she can choose consciously whether she will or will not be a mother"(Encyclopaedia Britannica, n.d). American reproductive rights have faced many transformations shifting between advancement and restriction over time. The 1960s marked a significant period in which social movements and legal milestones impacted the development of contraceptives and access to reproductive health services. Because of varying governmental regulations, progress for reproductive rights in the United States has not been linear since the 1960s due to various factors. These factors include the availability of contraception, legal protections for abortion, and surrounding controversy.

Pre-1960s

       Prior to the 1960s, the availability of contraception was limited due to the fact that it was seen as obscene with social and legal factors contributing to its restriction. This lack of access resulted in higher rates of unwanted pregnancies, limitation of reproductive autonomy, and unsafe abortions. For example, in 1873, Congress passed the Comstock Act which prohibited the distribution of contraceptives through the mail by classifying contraceptives as "obscene". PBS states, "The statute defined contraceptives as obscene and illicit, making it a federal offense to

disseminate birth control through the mail or across state lines" (Anthony Comstock's "Chastity" Laws, n.d.). At this time, the United States was the only Western Nation to have anti-obscenity laws criminalizing birth control in place (A Timeline of Contraception, n.d.). Contraception was heavily stigmatized and discussions surrounding sex and reproductive health were considered improper and taboo.

Many believed that contraception went against the natural order of things which had profound implications for family planning and individuals' choice of reproductive autonomy. Furthermore, access to contraception and accurate information about reproductive health was especially difficult for marginalized communities (Good, 2021). Women of color and those of lower income faced discrimination and socioeconomic disparities, making it all the more challenging to access reliable contraceptive methods and accurate education about sexual health (Prather et. al, 2018). This absence of availability of contraception further compounded the barriers for individuals to have control over their reproductive choices.

During the 1960s

In the 1960s, the introduction of available contraception transformed the landscape of reproductive health in American society by empowering individuals to make informed choices about their reproductive lives. One of the most profound changes that sparked a social and cultural revolution in reproductive health was the legalization of birth control in the United States. In 1960, the Food and Drug Administration (FDA) approved the sale of Enovid, the world's first commercially produced birth control pill (History, n.d.) This was one of the most pivotal events in the history of contraception by allowing women to plan and control their reproductive lives and make decisions about their own bodies and health. Margaret Sanger repealed the federal Comstock law by providing women with birth control information in order to control family size and end the cycle of women's poverty (Mundt, 2017). She believed that since women bore the burden of pregnancy and child-rearing, they should also have the right to control their fertility. Sanger opened the Planned Parenthood Federation of America, helped create "the pill", and her efforts led to the legalization and distribution of contraceptives in the United States (Michals, 2017). Planned Parenthood notes, "During the information wars between Congress, the FDA, the AMA, and the women, Planned Parenthood filled the gap with its own client information publications about the pill and developed its own medical standards and guidelines to ensure that all women who came to Planned Parenthood for the pill would receive balanced information about its risks and benefits" (Planned Parenthood, 2015). Overall, the introduction of available contraception in the 1960s provided a groundbreaking change in reproductive health and rights in the United States.

Post-1960s

Despite the advancement that was being made by legalizing contraception, in the last few years, the United States has receded in its progress of available contraception due to government restrictions. Mifepristone, a medication used for abortion, has been suspended by a Texas federal judge (Ollstein, 2023). This could compromise the safety of those seeking to terminate pregnancies and potentially result in individuals turning to illicit alternative methods. NBC News reports, "States trying to limit abortion from the moment of conception could also try to restrict access to Plan B and IUDs" (Bendix, 2022). Louisiana, Missouri, and Arizona have proposed laws that would ban abortion at fertilization. "IUD and Plan B are thought to prevent implantation, which could make these contraceptives illegal." Professor at the University of Virginia School of Law Naomi Cahn states, "If abortion is defined as preventing implantation of a fertilized egg, there is some fear that those contraceptives could be causing abortions" (Robinson, 2023). This increased regulation of reproductive laws further perpetuates the history of reproductive oppression in the United States. In summary, in recent years the availability of contraception has become limited due to the current state of political and social affairs in the United States.

Legal Cases

Regardless of the availability of contraception, legal protections for women seeking abortions are crucial to the progression of reproductive rights. Before the 1960s, legal rights surrounding abortion were significantly limited. Laws aimed to prohibit the termination of pregnancy by criminalizing abortion across different jurisdictions. Women who sought abortions often faced public humiliation due to societal stigma. In the novel, *When Abortion Was A Crime*, author Leslie J. Reagan writes, "The new mode of enforcing the criminal abortion laws brought women into contact with the criminal justice system in unprecedented ways… the state's methods used interrogation and the humiliation of public exposure to penalize women who had abortions" (Reagan, 1997). Newspapers would expose the names or pictures of women with the intention of shaming their sexual behavior, and women would risk legal repercussions if they were to seek an unregulated method of termination. To add on, medical professionals providing illegal abortion procedures also faced potential persecution for their involvement. The Feminist reports, "In the 1950s, about a million illegal abortions a year were performed in the U.S., and over a thousand women died each year as a result" (Norsigian, 1998). Desperate individuals were forced to turn towards dangerous methods, putting the lives and well-being of pregnant women in jeopardy. All in all, legal restrictions prior to the 1960s created an environment where women seeking safe abortions faced glaring challenges in terms of accessing the procedure itself and the potential consequences of their actions.

Court cases and legislative changes in the United States marked a significant advancement in the landscape of reproductive rights in the 1960s and 1970s. The landmark U.S. Supreme Court case *Griswold v. Connecticut* in 1965 recognized the constitutional right to privacy, as protected by the Due Process Clause of the Fourteenth Amendment, concerning childbearing decisions within marital relationships (Douglas, 1964). Furthermore, the case declared that Connecticut's

state ban on contraceptives was unconstitutional and thus was struck down. In 1973, the Supreme Court established that the right to privacy encompassed a woman's decision to terminate her pregnancy with the court case *Roe v. Wade*, recognizing a strict trimester framework for regulating abortion (Nunn et. al, 2022). The Court established that states were able to regulate abortion without banning it which allowed for a balance between a women's right to make decisions about her own body and protecting the potential life of a fetus. This transformed the legal structure surrounding reproductive rights and abortion in the United States and laid the groundwork for change in future decades. Subsequently, the Supreme Court case *Planned Parenthood of Southeastern Pennsylvania v. Casey* in 1992 reaffirmed the core holdings of *Roe v. Wade* but allowed for specific state regulations and proclaimed the "undue burden" test which modified the legal standard for evaluating the constitutionality of abortion restrictions (O'Connor et. al, 1991). Overall, these landmark court decisions in the 1960s and 1970s continued to influence subsequent legal battles about reproductive rights in the United States.

Despite reproductive rights having seen significant legal advancement in the past, legal rights have regressed in the United States in recent years. Supreme Court case *Dobbs vs. Jackson's Women's Health Organization* addressed whether the Constitution protected the right to abortion (Oyez, n.d.). *Dobbs* addressed the constitutionality of Mississippi's Gestational Age Act which banned most abortions after fifteen weeks of pregnancy with exceptions for fetal abnormalities or health emergencies. The Court upheld the law; On June 24, 2022, the U.S. Supreme Court overturned *Roe v. Wade* and *Planned Parenthood v. Casey*, eliminating the constitutional right to abortion and abandoning nearly fifty years of precedent. This decision marks the first time in history that the Supreme Court has deprived individuals of a fundamental right. America's political landscape reflects anti-abortion rhetoric as additional states act in accordance with the Supreme Court's decision to uphold Mississppi's fifteen-week abortion ban, passing similar provisions (Leff, 2022). The Center for Reproductive Rights states, "The Court's decision will likely lead to half of U.S. states immediately taking action to ban abortion outright, forcing people to travel hundreds and thousands of miles to access abortion care or to carry pregnancies against their will, a grave violation of their human rights" (The Center for Reproductive Rights, 2018). This devasting conclusion undermines the Constitution's promise to protect freedom and equality, revoking women's fundamental human rights. To conclude, the recent regression in terms of legality for reproductive rights has created a significant setback in the fight for equality and individual autonomy, specifically for those seeking abortion in the United States.

Public Perception

Aside from the legalities of abortion and other reproductive health rights, public opinion prior to the 1960s often emphasized restrictions on contraception, abortion, and reproductive making. Some believe these practices were deeply rooted in cultural and religious beliefs that

were seen as a violation of the natural order of things. This may be true, but the early 20th century's patriarchal refusal to allow women the right to control their reproductive health through shame and fear was likely an effort to strip women of their bodily autonomy. Additionally, women of color were disproportionately affected by the lack of reproductive healthcare which exacerbated existing disparities in terms of reproductive autonomy. Some members of the black community rejected birth control due to the belief that it was nothing more than a white plot to decimate the black race (Caron, 1998). Birth control was commonly disguised and sold as feminine hygiene products due to being immensely demonized socially (Johnson, 2021). In defiance of the American Medical Association's decision to withhold the approval of contraception, feminine hygiene manufacturers continued to distribute camouflaged contraceptive products to women (Sarah, 1994). Similarly, abortion was largely disapproved of as the procedure equated to taking a life based on societal perspective. The condemnation of reproductive autonomy resulted in limited discussions around family planning and reproductive health due to being taboo and seen as a moral transgression. In all, the prevailing social stigma associated with reproductive rights prior to the 1960s forced individuals to overcome social barriers in order to control their reproductive choices.

The 1960s paved the beginnings of change as society's views on reproductive rights began to shift and social movements emerged, advocating for greater autonomy and access to reproductive health resources. Public opinion became more accepting of contraception, abortion, and women's reproductive-decision making "with 54 percent saying abortion should be legal only under certain circumstances in 1975" (Goldstein, 2021). As the era of change progressed, social justice movements gained momentum fighting to ensure that women had the right to make informed choices about their bodies and reproductive lives. The Women's Liberation Movement, also known as the "second wave of feminism", sought to challenge and transform oppressive social structures of society ranging from reproductive autonomy, gender roles, sexuality, workplace discrimination, and more (Burkett, 2023). The introduction of the pill provided a catalyst for feminist activism exploding and sexual stereotypes being obviated. Women worked to redefine societal expectations by recognizing the systemic nature of gender inequality and asserting their sexual autonomy. Furthermore, reproductive movements aimed to address intersectional issues and acknowledge the experiences and voices of women of color. In 1983, the first National Conference on Black Women's Health Issues took place, giving birth to the National Black Women's Health Project (NBWHP), the first women of color reproductive justice organization (Silliman, 2004). These movements worked towards challenging the historical marginalization of women of color and recognized how reproductive rights are influenced by racial, economic, and political structures within society. Altogether, the 1960s represented a transformative period in terms of social opinion and perspective of reproductive rights in the United States.

However, in recent years, society's outlook on reproductive rights has experienced a regression, reverting towards more restrictive attitudes and policies. Anti-abortion violence has risen with pregnant individuals and abortion providers facing harassment due to waves of the

strictest abortion restrictions seen in decades. The National Abortion Federation revealed that in 2020 violence and disruption–specifically, reports of assault and battery–against abortion clinics increased by 125% compared to 2019 (National Abortion Federation, 2020). Abortion providers are continuing to be threatened with the number of death threats increasing by the year. The politicization of abortion rights has aided this increase in violence. Even today, the majority of Americans support access to abortion in all or most cases, but former President Trump's appointment of extremely conservative justices to the Supreme Court of the United States has allowed a vocal minority (anti-abortion Americans) to gain both a national platform and control of the law (Hartig, 2022).

Additionally, women of color in comparison to their White counterparts continue to be disproportionally affected by the significant challenges and ongoing debates surrounding reproductive healthcare. The National Women's Law Center writes about how a local anti-abortionist group has targeted West Virginia's only black legislator with racist threats due to her support of legislation that would obstruct all abortion restrictions in the state (Leff, 2022). Since the Supreme Court's ruling on Roe, many states have already outlawed abortion services and more are expected to do so in the future. The Kaiser Family Foundation describes that "many of these states are in the South, which has large shares of Black and Hispanic women, the Plains which has a large Indigenous population, and the Midwest." Accessing abortion for women of color will become increasingly difficult with the absence of laws protecting abortion in states like these. The KFF reports, "More than half of abortions are among women of color...In 2019, almost four in ten of abortions were among Black women (38%), one-third were among White women (33%), one in five among Hispanic women (21%), and 7% among women of other racial and ethnic groups." Denying people of color access to comprehensive reproductive healthcare displays the deeply-rooted racist practices surrounding the healthcare system in the United States. Moreover, anti-abortionists spread propaganda to campaign against abortion and seek to pack federal courts with justices in favor of reproductive healthcare limitations. The New Yorker details the link between the United States Capitol attack in January of 2021 and anti-abortion extremism discussing how "John Brockhoeft, who was convicted of firebombing a Planned Parenthood clinic in Cincinnati, in 1985, and of conspiring to bomb another abortion clinic in Pensacola, in 1988, live-streamed from outside the Capitol." Many view anti-abortionism as synonymous with patriotism as states begin to enact laws of near-total ban on abortion procedures. As a result, although public opinion on reproductive rights and abortion became less conservative during the 1960s and 1970s, society's viewpoints and standings on this controversy have regressed in recent years.

Conclusion

In conclusion, reproductive rights in the United States have witnessed both progress and setbacks from before the 1960s until modern times. While the 1960s represented a period of progress for women across the country compared to earlier in the 20th century, the advancement of reproductive rights has since stagnated in various areas. These areas include the availability of

contraception, legal protections for abortion, and surrounding controversy. Following the words of Margaret Sanger, unless the regression of reproductive rights in the United States is halted, women will continue to be stripped of their individual autonomy and therefore their ability to live freely in this country.

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Investigating the Role of Epigenetics in Cancer By Anushree Choudhury

Abstract

Cancer, a disease as unique as its host, arises from the interplay of genomic and environmental factors, with the epigenome adding a layer of complexity. Epigenetic elements such as DNA methylation, histone modifications, and non-coding RNAs are pivotal in cancer initiation, progression, metastasis, and the development of drug resistance. In the past decade, epigenetics, once considered a contributor to cancer, is now viewed as a potential solution, given its reversible nature. Epidrugs transform the cause into the cure, forging a path to correct epigenetic alterations such as oncogene activation or TSG suppression in order to restore normal cellular activity.Some cancer, notably breast, lung, and prostate cancer, which are particularly susceptible to epigenetically induced carcinogenesis. The unique and individualised nature of each cancer underscores the importance of understanding the epigenetic landscape in order to tailor effective treatment strategies.

Introduction

The term "Epigenetics" was formulated by British developmental biologist & paleontologist C . H. Waddington by combining the two words "epigenesis" and "genetics" (Hurd, 2010). It refers to the relation between an organism's genetic makeup (genotype) and how its genes are expressed, eventually determining observable qualities (phenotype). These epigenetic alterations have no effect on the underlying DNA sequence, but impacts how genes are transcribed. The term 'epigenome' refers to modifications, which include DNA methylation patterns, histone alterations, and microRNA variations. Interestingly, these epigenetic modifications are influenced by extrinsic factors like lifestyle, nutrition, and stress. They have the potential to disrupt the normal regulation of genes, leading to alterations in protein production, which in turn, can contribute to various diseases, including cancer. Epigenetic dysregulation activates the oncogenes and inactivates the tumour suppressor genes (Pathak et al.,2023).

Cancer is characterised by uncontrolled cell growth and the loss of critical features such as contact inhibition and apoptosis (cell death). Its development is driven by the disruption of essential cellular pathways governing processes like the cell proliferation, differentiation, and programmed cell death. Cancer cells outcompete healthy ones by accelerating nutrient consumption, increasing metabolic rates, and promoting the formation of abnormal blood vessels through angiogenesis. To effectively combat cancer, it's essential to address its root causes through epigenetic therapies like epidrugs supplemented by chemotherapy, immunotherapies, etc. While ongoing research strives to unravel the precise mechanisms through which epigenetic alterations initiate and advance carcinogenesis, establishing a clear causal link remains a

challenge. Additionally, many biomarkers influenced by epigenetic changes are not yet definitely recognized as cancer triggers, as they can also result from the presence of cancer. In summary, understanding and targeting the fundamental drivers of cancer. Epigenetic alterations are leads for distinctive markers for cancer detection, therapy and prognosis.

This review addresses a notable knowledge gap in cancer research by shifting the predominant focus from genetics to epigenetics. Historically, cancer research has primarily concentrated on genetic factors, leaving the vital role of epigenetics in the shadows. Epigenetic pathways, which include DNA methylation, histone modifications, and non-coding RNA regulation, are increasingly becoming recognized as key factors to cancer initiation, development, and therapeutic resistance. Understanding the reversible and dynamic nature of epigenetic changes, offers the potential to revolutionise cancer research and therapy, transforming what was once considered a contributing factor into a promising solution. This paper fills an existing gap in the literature by emphasising the essential role of epigenetics in cancer research. By doing so, it broadens our understanding of cancer progression and therapy, highlighting the transformative potential of epigenetic insights, and contributing to the evolving landscape of cancer diagnosis and treatment.

1. Types Of Epigenetics Modifications:

1.1 DNA Methylation

DNA methylation is a crucial epigenetic process that modifies the methyl group at the fifth carbon of cytosine's pyrimidine ring, creating 5-methylcytosine (5mC), which controls the expression of genes (Jacobsen et al., 2010). This covalent alteration recruits proteins or prevents transcription factors from binding, which directly affects gene expression.

One crucial aspect of DNA methylation involves CpG islands, where a methyl group is added to the C5 position of the cytosine ring in the context of cytosine-guanine pairs (CpG). When promoter sequences in CpG islands become hypermethylated, this often leads to the inactivation of tumour suppressor genes. Tumour suppressor genes play a vital role in regulating various cellular pathways involved in cancer prevention, including those related to cell growth, cell proliferation, and apoptosis.DNA methyltransferase (DNMT) is an enzyme that regulates DNA methylation patterns. DNMT1 is primarily involved in maintaining existing DNA methylation patterns, while DNMT3a and DNMT3b establish new methylation patterns. In cancer, hypermethylation of promoter regions is a well-documented epigenetic change found in virtually every type of human neoplasm. This hypermethylation is associated with the inappropriate transcriptional silencing of genes that are important for tumorigenesis. These genes include O6-methylguanine-DNA methyltransferase (MGMT), which encodes a critical DNA repair gene, cyclin-dependent kinase inhibitor 2B (CDKN2B), which encodes p15, a cell-cycle regulator, and RASSF1A (Park et al., 2008).

According to Knudson's two-hit hypothesis, tumorigenesis results from the silencing of both alleles of tumour suppressor genes.One allele is frequently already mutated in those with a hereditary history of cancer, and DNA methylation can mute the other allele.According to

Knudson's model, unless both alleles of a tumor suppressor gene are inactivated, the phenotypic effect of tumour suppressor gene loss will not be seen (Wang et al., 2019). In cancer, the Warburg Effect is a well-known hallmark. It involves cancer cells consuming significantly more glucose and producing lactate even in the presence of oxygen. This metabolic alteration supports the rapid growth and energy demands of cancer cells (Zhu et al., 2020).

Hypomethylated regions in the genome have an unusually open nucleosome configuration and an abnormal acetylation of histone lysines. In contrast, abnormal nucleosomes positioned over the transcription start sites of silenced genes are associated with DNA hypermethylation in promoter CpG islands (Deaton et al.,2011). As per study conducted by Figeroa et al. & Noushmer et al.,2010, whole-exon sequencing of various human cancers, including leukemias, lymphomas, ovarian, renal, and pancreatic cancers, as well as rhabdomyosarcoma, has revealed a high occurrence of mutations in specific genes.Some of the genes include ARID1A, DNMT3A, EZH2, IDH1, MLL, PBRM1, SNF5, and VHL.

1.2 Histone modification

DNA is coiled around basic histone proteins resulting in a DNA-protein complex called chromatin. Both heterochromatin and euchromatin are histone proteins that control the rate of transcription. Euchromatin is a less compact and loosely packed form of chromatin. It is associated with a higher transcriptional rate because genes in euchromatin are more accessible for transcription. On the other hand, Heterochromatin is tightly packed and associated with a reduced transcriptional rate because the chromatin shape hinders access to the underlying DNA (Zhao et al., 2018). Thus, the control of gene expression is greatly aided by histone alterations. Dysregulation can lead to a disruption in homeostasis gain or loss of function of genes, overexpression, suppression by promoter hypermethylation, chromosomal translocation, or mutations of the histone-modifying enzymes/complexes or even the modification site of the histone (Lawrence et al., 2016) & (Audia et al., 2016).

Histone proteins can be modified via acetylation, methylation, and phosphorylation. Acetylation is the process of adding acetyl groups to lysine residues on histone proteins, most notably in the N-terminal tails. Acetylation reduces the interaction between histones and DNA by neutralizing the positive charge of lysine. This results in a more open and accessible chromatin structure, allowing for increased gene transcription. Histone acetyltransferases (HATs) are enzymes that catalyze the addition of acetyl groups to lysine residues.

Methylation of histones can occur on lysine and arginine residues and has varying effects on gene expression depending on the specific histone and the level of methylation. Methylation has the ability to either stimulate or suppress gene transcription. For example, trimethylation of histone H3 at lysine 4 (H3K4me3) is associated with active gene transcription, while trimethylation at lysine 9 (H3K9me3) is associated with gene repression.

Phosphorylation of histones involves the addition of phosphate groups, often at serine or threonine residues. Phosphorylation plays a role in various cellular processes, including DNA

damage repair, cell cycle regulation, and gene transcription. It can modulate the binding of other proteins to histones (Park et al., 2020).

According to a study conducted by Srivastava, et al., 2022 it was discovered that post-translational modifications (PTMs) of histones, such as acetylation, methylation, or phosphorylation, also contributed to the development of tumors.

Studies to understand lymphomagenesis demonstrate that mutations in genes responsible for modifying histones or in related transcription factors can disrupt the normal patterns of histone modifications, contributing to the development of lymphoma.The examination of recurrent mutations in B-cell Non-Hodgkin lymphoma, which comprises more than 90% of all lymphoma cases, has demonstrated that somatic mutations frequently target genes linked to histone modification. The most often mutated gene is the MLL2 gene, often referred to as histone-lysine N-methyltransferase (KMT2D), which has several single nucleotide variants spread out over the entire sequence. MLL2 is a significant histone methyltransferase in mammals, playing a role in mono-methylation H3K4 and functioning as a tumor suppressor gene in non-Hodgkin lymphoma. Another gene affected by mutations in this context is MEF2B, a transcription factor involved in calcium-regulated histone acetylation and methylation (Yang et al., 2022). The most prevalent mutation in MEF2B leads to changes in the amino acid D83V, which doesn't impact DNA interactions but does disrupt interactions with certain repressive complexes, including the HUCA complex and HDAC class IIa members. This disruption results in abnormal expression of histone markers at H3K27 (Yang et al., 2022).

1.3 Non-coding RNA

Approximately 2% of DNA is dedicated to encoding protein-coding genes, while the remaining 98% is considered non-coding, historically viewed by the scientific community as junk or without a recognized function (Pathania et al., 2022). Most non-coding RNA emerges from this junk DNA and does not code for any functional proteins.

Non-coding RNAs (non-coding RNAs) that are not translated into proteins are classified as housekeeping non-coding RNAs and regulatory non-coding RNAs. According to size, RNA with a regulatory function is primarily separated into two groups: long non-coding RNA (lncRNAs) and short-chain non-coding RNAs (siRNAs, miRNAs, and piRNAs) (Zaratiegui et al., 2007) & (Ponting et al., 2007). Recent research has demonstrated that non-coding RNAs are important for epigenetic modification and can control chromosomal and gene expression to regulate cell differentiation (Costa, 2008, Amaral et al., 2008, Ghildiyal et al., 2009 & Yu H, 2009).Non-coding RNAs that are not translated into proteins are classified as housekeeping non-coding RNAs and regulatory non-coding RNAs. Short-chain non-coding RNAs (siRNAs, miRNAs, and piRNAs) and long non-coding RNAs (lncRNAs) are the two main categories of RNA with a regulatory role based on size.(Zaratiegui et al., 2007; Ponting et al., 2007).

According to a 1969 theory of gene regulation by American molecular biologist Roy John Britten and developmental biologist Eric Harris Davidson, repetitive non-coding sequences may code for non-coding RNAs that function as regulatory mediators to transmit signals and influence

gene translation (Wolter et al.1969). ncRNA have several important functions such as signalling pathways responsible for cancer initiation and progression, gene expression through chromosomal modulation, transcriptional regulation, and post-transcriptional modifications (Zhou et al ., 2016). ncRNA are divided into various classes based on their size and functions; miRNA and piRNA(around 22 nucleotides) function in RNA suppression and transposon activity in germ line and somatic cells. lcRNA modulates gene expression at mRNA stability, transcriptional, and post-transcriptional levels (Yao et al .,2019). Recent research has demonstrated that non-coding RNAs are important for epigenetic modification and can control chromosomal and gene expression to regulate cell differentiation (Costa, 2008, Amaral et al., 2008, Ghildiyal et al., 2009 & Yu H, 2009).

Cancers can develop as a result of either oncogene overexpression or tumor suppressor gene inactivation. The interplay of epigenetics and genetics to give rise to cancer phenotype is called carcinogenesis. This is often linked to uncontrolled cell proliferation, loss of contact inhibition, loss of the ability of apoptosis, and the acquisition of the property of angiogenesis. Tumour suppressor genes can become inactive in three ways: through disabling mutations, gene loss, or somatic heritable epigenetic changes that switch off the gene's function without altering its DNA sequence (Pathak et al., 2023). Interestingly, CpG island hypermethylation has been associated with the silencing of genes involved in cell proliferation and tumor suppressors. Examples of genes where hypermethylation is linked to carcinogenesis are the Glutathione S-transferase P (GSTP1) in prostate cancer and the BRCA1 gene in breast cancer (Esteller et al., 2000).

Epigenetic biomarkers are not only linked to tumor initiation but also have a significant role in cancer progression. For instance, EZH2(enhancer zeste homolog 2)- a histone methyltransferase and a key part of PRC2, is responsible for adding three methyl groups to histone H3 at Lysine 27 (H3K27), a process known as trimethylation. This modification is crucial for controlling gene expression through epigenetic mechanisms and is linked to increased tumor growth.EZH2 promotes cell survival, proliferation, epithelial to mesenchymal, invasion, and drug resistance of cancer cells and has decisive roles on immune cells affecting the tumor microenvironment (Gan et al., 2018). Long Non-Coding RNA (lncRNA): Long non-coding RNAs, which do not code for proteins, can interact with DNA, RNA, and proteins, influencing various cell processes, including cell differentiation and regulated cell death like ferroptosis. In non-small cell lung cancers, lncRNAs suppress cancer development through ferroptosis pathways.

2. Epigenetic Alterations in different Cancers
2.1 Breast cancer

Breast cancer encompasses a diverse group of diseases originating from the breast, marked by biological and molecular variations. BRCA1/2, classified as tumour suppressor genes, have associations not only with breast cancer but also prostate and pancreatic cancers. These genes play crucial roles in cell cycle regulation, chromosomal modifications, DNA repair, and apoptosis (Feng et al,.2018). They are especially important for DNA repair processes, including

homologous recombination and nucleotide excision repair, in response to chemotherapy-induced DNA damage.

Furthermore, epigenetic alterations, such as DNA methylation and changes in chromatin structure, are detected early in cancer development..

A trend in global hypomethylation is observed, however, the number of genes which are hypomethylated are significantly lesser such as *FEN1*, *BCSG1*, *PLAU*, *IGF2* and *CDH3. On the contrary,* over 100 genes which play involved in various cellular processes, including cell-cycle regulation, apoptosis, tissue invasion, metastasis, angiogenesis, and hormone signalling undergo hypermethylation such as CCND2 and p16ink4A/CDKN2A (cell cycle regulators), APC, TWIST, and HOXA5 (apoptosis regulators), and ERα and PR (hormone regulators).

Secondly, due to histone modification, gene expression is regulated, for example histone demethylases, such as Pygo2, JMJD2B, and LSD1, are implicated in breast tumorigenesis. They influence various cellular processes, including transcriptional activation and cell cycle progression.

Long non-coding RNAs and microRNAs are recognized as pivotal contributors to breast cancer progression, leading to intratumoral heterogeneity.Since miRNA are downregulated, leads to reduced levels of let-7 family and miR-15/16 in breast cancer contribute to heightened tumorigenicity and abnormal BCL2 expression, while the frequent amplification of miR-21 is associated with increased invasiveness and metastasis to the lungs (Chen et al.,2014). Additionally, exposure to environmental factors like mineral dust, tobacco smoke, arsenic, and silica can stimulate the expression of the mineral dust-induced gene (MDIG). MDIG promotes cell proliferation, cell cycle progression, and anti-apoptotic behaviours in various cell types, indicating its pro-proliferative properties (Thakur et al., 2022). However, MDIG has a dual role in breast cancer, acting as a facilitator in the early stages of cancer development due to its pro-proliferative characteristics but serving as an inhibitor in later stages, where it exhibits metastasis-inhibitory features. Distinct patterns of reprogramming are observable from the early stages of ductal hyperplasia to invasive carcinoma. These epigenetic effects extend beyond cancer cells, also manifesting in normal cells, indicating a broader field effect (Feng et al., 2018).
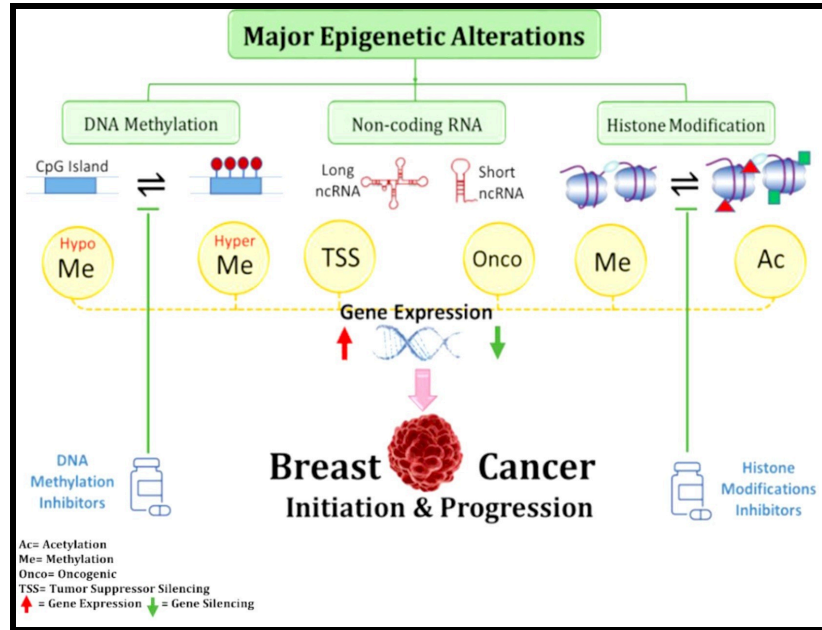
Figure 1: Diagram depicting CpG island methylation and histone changes that result in oncogene and tumor suppressor gene dysregulation. (Source: Gulab Sher et al.,2022).

2.2 Lung cancer

Lung cancer displays significant diversity in its development, attributed to factors like the pre. sThe control of EMT and cancer stem cells in lung cancer is greatly impacted by histone modifications and non-coding RNA alterations. Epigenetic alterations, particularly histone modifications, play a pivotal role in lung cancer, impacting various aspects like cell growth, invasion, metastasis, cell death, and cell cycle regulation. EMT, a process where epithelial cells transform, losing polarity and adopting mesenchymal characteristics, exacerbates cancer and promotes metastasis (Baghel et al., 2023). Furthermore, significant signalling pathways such as the NF-kB, Hedgehog, and ERK families are impacted by epigenetic dysregulation in lung cancer (Shi et al., 2019).
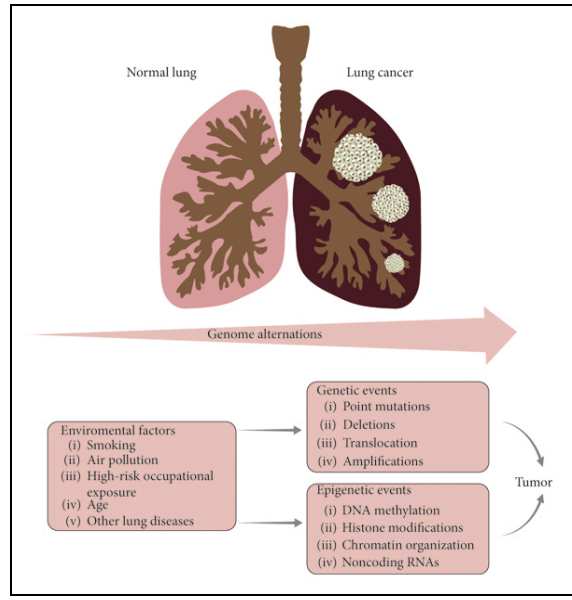
Figure 2: Genetic and epigenetic alterations linked to tumorigenesis
(Source: Shi et al., 2019)
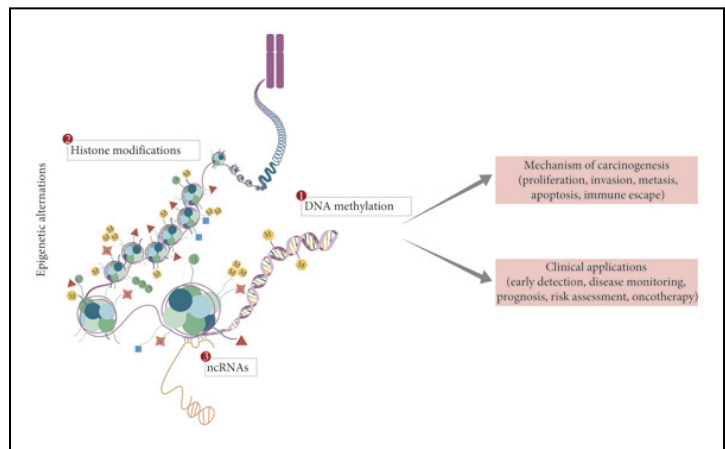
Figure 3: Landscape of epigenetics and its clinical application
(Source : Shi et al., 2019)

2.3 Prostate cancer

Prostate cancer is the uncontrolled proliferation of cells in the prostate, a gland in the male reproductive system located directly below the bladder. Epigenetic modifications, which include changes in DNA methylation, histone modifications, and nucleosome rearrangements, are important at all stages of prostate cancer (PCa) development and progression. These mutations cause tumor-suppressor genes to be silenced, oncogenic drivers to be activated, and therapeutic resistance to emerge (Pathak et al., 2023). In prostate cancer, over 50 genes consistently exhibit abnormal hypermethylation, impacting various cellular functions such as cell cycle regulation, apoptosis, hormonal responses, DNA repair, signal transduction, tumor invasion, and suppression.

Noteworthy genes like APC, CCND2, GSTP1, RARβ2, RASSF1A, and PTGS2 frequently demonstrate promoter methylation in PCa (Lam et al., 2020). A promising avenue in treating prostate cancer involves targeting epigenetic pathways associated with androgen receptors (Sarkissyan et al., 2014). In particular, EZH2, an essential part of the polycomb repressive complex (PRC2) that modifies H3K27me3 to repress genes, has been found to be a viable target for PCa therapy.

3.Treatment

Epigenetic modifications do not only initiate carcinogenesis and its progression but also help neoplastic cells develop resistance to drugs hence rendering therapies against cancer futile. In CpG-rich islands, cancer cells like TSG experience hypermethylation and are inactivated. On the other hand, there is a genome-wide hypomethylation activating oncogenes. DNA methyltransferase is the focal target to restore the normal methylation levels by activating TSGs and deactivating oncogenes. There are two classes of DNMT inhibitors- Nucleoside analogs and non nucleosides (Pathak et al,.2023)

Azacitidine and Decitabine (FDA-approved), these two induce methylation to activate TSGs.Considering both the achievements and limitations of azacitidine and decitabine, researchers have developed prodrugs based on these compounds as advanced(DNA methyltransferase) DNMT inhibitors. Nucleoside analogs, featuring altered cytosine rings, can be integrated into newly formed DNA, forming a covalent bond with DNMTs. This interaction hinders the transfer of methyl groups to the hemimethylated DNA in offspring cells, resulting in widespread demethylation and subsequent degradation of DNMTs through the proteasomal pathway.

These next-generation inhibitors offer improved pharmacokinetic characteristics. As drugs are designed to target specific epigenetic abnormalities, they represent a pathway toward the future of personalized medicine. This means that individuals with particular epigenetic errors can receive custom-made epi drug treatments tailored to their specific condition (Furtabo et al., 2019).

According to Rodríguez-Paredes et al. (2011) and Salarinia, R. et al. (2016), epigenetic drugs are chemicals that change the structure of DNA and chromatin, encouraging the disruption of transcriptional and post-transcriptional modifications. They do this primarily by controlling the enzymes required for these modifications' establishment and maintenance, which reactivate genes that are epigenetically silenced and that repair DNA. The primary method by which epidrugs work on the enzymes required for the creation and preservation of epigenetic changes is by inhibiting DNMTs and HDACs (Paredes, Rodriguez, and others, 2011).

Conclusion

Cancer is a highly individualized disease, making one-size-fits-all treatments ineffective. The causes of cancer are often complex and not well-defined, with epigenetics being one contributing factor. To effectively treat cancer, it is essential to diagnose it early using biomarkers and create a personalized treatment plan, known as precision medicine. Recently, there has been a

growing focus on targeting epigenetic changes in cancer treatment. These changes can both trigger cancer growth and contribute to challenges like diverse tumor characteristics and resistance to drugs. However, the reversibility of epigenetic modifications presents both a challenge and an opportunity. They can be targeted and reversed effectively through approaches like combination therapies, using bacteria for therapy, or employing CRISPR technology. Moreover, the topic of epigenetics and cancer research is relatively new and offers exciting research opportunities, such as the creation of more precise biomarkers for early cancer detection and growth prediction.

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Genetic Engineering of Viruses to Infect Cancer for Human Health By Li, Leo.[1] and Greenwald, E.[2]

Abstract

Genetic engineering is the perturbation of DNA or RNA for research applications, diagnostics and addressing medical needs in health. Genome editing is the modification of genes in a living organism, which can be used, for one example, in an attempt to fight genetic diseases. DNA is the genetic makeup of any organism and can be edited with enzymes, which will cut the nucleic acid, potentially altering the function of the specific gene that was edited. CRISPR is a revolutionary genetic engineering tool that utilizes one of these enzymes that can alter genomes with ease compared to previous tools. It consists of a Cas enzyme paired with a guide RNA and can cut a target locus in the DNA. Cancer remains one of the deadliest genetic diseases to the global human population. Although new treatments have come far, millions die from cancer every year. Viruses are also large killers, but we can alter the DNA of viruses and repurpose them to fight cancer cells. With oncolytic virotherapy, the repurposing of viruses as a therapeutic to attack cancer, we will be able to use certain genetically-engineered viruses to specifically infect cancer cells, helping work towards the eradication of cancer. Genetic engineering is key to the advancement of human health because, with the perturbation of organisms and viruses, we will be able to improve human health. CRISPR's ability to accurately edit genes allows the applicability of virotherapy to fight cancer to become a reality. Being able to convert viruses into a cancer fighting treatment will require further clinical trials as well as additional discoveries of which genes to edit in order for viruses to safely target cancerous cells and avoid healthy ones. If researchers are able to successfully create a virus for cancer treatment, it will only prove CRISPR's applicability as well as reliability in other genetic diseases beyond cancer.

Keywords

Genetic engineering, Cancer, Viruses, CRISPR/Cas9, Therapeutics, Genome editing, Virotherapy

Introduction

Cancer kills millions of people every year, making it one of the world's deadliest diseases.[1] Cancer is a state of uncontrolled cell division and proliferation caused by genetic mutations in genes that, under healthy conditions, prevent unhealthy cell growth.[2] Cancer-causing mutations often influence the genes responsible for cell cycle checks, which are important for ensuring that only healthy cells are growing and potentially unhealthy or cancerous cells are stopped from continuing to divide.[2] Therefore, there are two types of genes most commonly mutated in cancer cases: oncogenes and tumor suppressor genes, which have opposing functions in the cell. Under healthy conditions, oncogenes promote cell growth, and tumor suppressor genes prevent unwanted or excessive cell growth. In cancer conditions, oncogenes are mutated to act too much, and/or tumor suppressor genes are not active enough.[3]

Current treatments, such as chemotherapy or surgery, are effective to a limited extent. Chemotherapy refers to a class of drugs that inhibits cell growth, specifically in fast-growing cells.[4] It is commonly used in treating cancer, but has severe side effects, suppresses the immune system, causes mutations, and cancer cells sometimes become resistant to chemotherapy drugs, making it ineffective over time.[5] Surgeries are only effective during early stages of cancer before it spreads, or metastasizes, as removing the cancerous cells is only effective when they are all in one place and therefore all removed by the surgery.[6] Both of these treatment options become ineffective as cancer spreads and mutates, so there is a crucial need for more effective, complete treatment options against cancer.

Genetic engineering is the perturbation of nucleic acids, DNA or RNA, for research applications, diagnostics and addressing medical needs in health. Genome editing is the modification of genes in a living organism in an attempt to fight genetic diseases, such as cancer.[7] DNA is the genetic makeup of any organism and can be edited with special classes of nucleases that cut the nucleic acid, altering the function of the specific gene that was edited.[8] Clustered Regularly Short Palindromic Repeats (CRISPR) genome editing is a revolutionary genetic engineering tool, discovered in 2012, that can alter genomes with specificity, efficiency, and ease compared to previous tools, including recombinant DNA technology. This technology consists of a Cas enzyme (Cas9 is the Cas enzyme specifically used to cut double-stranded DNA) paired with a guide RNA and can cut targeted DNA.[9]

Viruses are non-living pathogens with a natural delivery method for putting new nucleic acid into cells and some types of viruses integrate that nucleic acid into the host genome.[10] Using genetic engineering, we can alter the DNA of viruses and repurpose them into fighting cancer cells. With this tool known as oncolytic virotherapy, we could be able to use certain viruses to only infect cancer cells, helping work towards the eradication of cancer.[11] Genetic engineering is key to the advancement of human health. With certain modifications or supplements into our body, immune response towards tumors can be enhanced and magnified, creating more effective resistance against cancer. Although still in research, CRISPR and genetic engineering in concert with oncolytic virotherapy in the clinical field provide much-needed hope as the potential to cure cancer remains on the horizon.

CRISPR/Cas9 for genome editing

The CRISPR/Cas9 system was discovered from bacteria's natural defense mechanism against viruses. Through evolution, prokaryotic cells evolved an immune defense mechanism, CRISPR, in order to protect the cell from viral infections. CRISPR sequences in the bacterial genome were identified when they noticed short, palindromic repeats interspaced with other sequences, which they later realized to be viral.[9] Those in-between sequences were actually transcribed into RNA that was used to guide a newly identified CRISPR-associated enzyme, Cas9 (an endonuclease-an enzyme that cleaves nucleotides- guided by RNA), to the complementary sequence in the viral genome.[9] In the bacteria, two types of short RNA are produced when virus DNA is detected, trans-activating CRISPR RNA (tracrRNA) and CRISPR (crRNA).[9] TracrRNA base-pairs at the end of crRNA, known as the complementary strand, creating a structured

complex that helps Cas9 recognize what DNA to edit.[9] The two strands form a guide RNA (gRNA), which matches the virus DNA. The RNAs form a complex with a nuclease called Cas9, a type of enzyme that can cut DNA based on sequence complementarity to the guide RNA, making it a sequence-specific system that therefore targets specific places in the genome.[9] When the guide RNA matches with the DNA, Cas9 cuts the viral DNA, preventing a viral infection.[9,12] From this, researchers realized that the guide RNA can be engineered so Cas9 cuts any DNA sequence, not just the bacteria-infecting viruses it was evolutionarily intended to defend against.[9] The CRISPR/Cas system locks onto the protospacer adjacent motif (PAM), a short sequence of DNA at the site of cleavage.[9,13] Using the guide RNA, Cas9 is able to recognize which DNA sequence to cut because of complementary base-pairing rules (adenine-thymine/uridine, guanine-cytosine),[14,15] completely revolutionizing genetic engineering.[9] CRISPR is highly accurate because the guide RNA is sequence-specific and is limited to a small number of sites.[9] Previous genetic engineering tools such as Zinc finger nucleases (ZFN) and Transcription Activator Like Effector Nucleases (TALEN) were more inaccurate and ineffective in editing DNA compared to CRISPR, making it one of the most groundbreaking discoveries in genome history.[9,12]

After cleavage, researchers can either allow nonhomologous end joining (NHEJ) to repair the DNA, disrupting any function of this DNA sequence. NHEJ is a natural method for cells to fix damaged DNA. NHEJ combines the two ends of the broken DNA strand, gluing them together.[12,16] In this case, cleaving the DNA causes gaps between the DNA and NHEJ closes the void by reconnecting the two broken ends, also known as "knock-out," by adding or remove random base pairs, causing what is known as a frameshift.[12] Due to these frameshifts, NHEJ ruins the codon sequences, disrupting gene functions and silencing it. For research purposes, nonhomologous end joinings can be beneficial.[17] These mutations often disrupt the functions of the targeted DNA sequence, allowing researchers to study the role of the gene, because they can observe what happens or possibly what goes wrong without the function of that gene. Homology-directed repair (HDR) uses a single strand of DNA as a "template" to teach the cell to repair its own DNA.[12] By using this template, it specifically guides the cell to use certain base pairs, also known as "knock-in," ensuring accuracy of desired base pairs. With HDR, we can add full sets of genes, avoiding the randomness in NHEJ.[18] Using CRISPR and these two methods of genome editing, we can disrupt genes in cells in the lab, allowing researchers to investigate the functions of those genes in the cancer context. This can be applied, for example, to the identification of drug resistant genes, improving the effectiveness of current cancer treatments.

There are many potential applications of CRISPR in cancer as cancer is a genetic disease. Cancer is caused by mutations that promote uninhibited, uncontrollable cell growth. Inhibition of specific genes can cause apoptosis, which can fight cancer.[11] Apoptosis is programmed cell death caused by some problem in the cell, such as damaged DNA during mitosis or viral infections.[19] In one study, the knock-out and inhibition of the Myeloid Cell Leukemia (*MCL-1*) gene induced apoptosis in Burkitt lymphoma cells, a cancer in the lymphatic system (part of the immune system).[20] In healthy cells, the *MCL-1* gene produces the MCL-1 protein that inhibits apoptotic

proteins, preventing cell death.[20] MCL-1 controls unnecessary apoptosis in cells, but when a cell becomes cancerous, it will evade apoptosis and divide uncontrollably,[2] leading to a cancer, which is unhealthy for the organism. Mechanisms to promote cell death in cancer cells are crucial to fighting cancer. Inhibiting this gene can allow cancerous cells to commit apoptosis before spreading and becoming a tumor.[21] Additionally in colon cancer, protein kinase C (PKC)--an enzyme in a phosphorylation signaling pathway–was inhibited by a cancer-causing mutation.[22] *PKC* has been recognized as a tumor suppressor gene, so because of its inactivation, a tumor developed[21]. CRISPR/Cas9 may be harnessed to correct this mutation, allowing it to fight tumors. Furthermore, stromal cells make up connective tissues between organs and modulate inflammation in the body.[23] However, in cases of tumor growth, normal stromal cells have been found to have a symbiotic relationship with cancer cells, allowing tumor growth.[23] For example, in pancreas cancer, the vitamin D receptor in stromal cells promotes tumor growth. Cas9 can knock down genes like the vitamin D receptor to make cancer more treatable.[21] One main benefit of edited stromal cells is that they do not affect the rest of the body, ensuring no side effects.

CRISPR/Cas9 genome editing may be the key to the future of the cancer field as it offers many promising solutions on fighting this deadly killer. One of the key issues with cancer is its variability. The reality is that every tumor in every patient is different and has different genetic mutations. In other words, researchers would need to discover the correct guide RNA sequence to use in every scenario. As mentioned above, if the patient's cell had a mutation that caused the inhibition of *PKC*, researchers and oncologists would have to work together in order to discover which specific sequence of the DNA caused this inhibition. Unfortunately, each individual case may be a result of different mutations, even within the same type of cancer, which is where CRISPR comes into effect. Even niche mutations that are rare can be resolved via CRISPR as long as researchers are able to identify which mutation caused the tumor. By specifically targeting the cell type that is developing cancer with the Cas9 enzyme (alongside the gRNA and donor sequence), it can nullify and delete or correct mutations, returning the cell into its healthy state. The only key problem that remains is the safety and efficacy of Cas9 within drugs and how to deliver these enzymes to the cells that need it. Such methods can be optimized through testing of artificial cells resembling a patient's tumor and later, clinical trials to ensure the safety of not our patients, but the safety of the participants in these clinical trials.

Oncolytic virotherapy

Oncolytic virotherapy is a new approach being investigated for potential clinical purposes against cancer. It relies on genetically modified viruses to attack and kill cancer cells. While some viruses cause illness and can even lead to cancer, such as Human Papilloma Virus, a modified HPV virus was surprisingly found to promote tumor regression.[23] Randomly, many patients were discovered to have tumor regression after certain viral infections. The first report of using virotherapy was in 1949: 22 patients with Hodgkin's disease, a lymphatic cancer, were treated with tissue extracts containing hepatitis [25] (note: The different types of hepatitis were discovered in the late 20th century[26], therefore it is unknown which hepatitis virus was used in this case). It appeared that researchers were well aware of the lower prevalence of Hodgkin's disease whenever

the patient had some sort of liver disease. Although not specifically stated, we believe that hepatitis was used to treat these patients because researchers were aware that patients who had liver disease had a lower prevalence and severity of Hodgkin's disease.[27] Over the course of the next several decades, from the 1950s-80s, several clinical trials attempted to use viruses to fight cancer, but viruses were not deemed effective against cancer because of the lack of the ability to clinically control the virus because it does not specifically target cancer cells.[11] However, with our current understanding of cancer, researchers discovered that most cancer cells had impaired protection against viruses.[28] This is because some cancer cells express higher levels of receptors, making it easier for viruses to infect the cell.[29] This inspired virotherapy, a technique where viruses are engineered to specifically target cancer cells. Every virus has its own method of infection, each controlled by different genes in the virus and different protein interactions on the surface of the infected cell.[30] Because of this, there isn't yet a definitive solution to cancer using virotherapy.

Regardless, a promising discovery was made in the late 1990s. Researchers wanted to engineer a virus which would only target cancer cells, allow it to reproduce and infect other tumors.[11] The main challenge was preventing viral infections to our healthy cells, yet maintaining its effectiveness in infecting and killing cells.[11] That problem was solved with TVEC,[11] a double mutated herpes simplex virus (HSV)-1.[31] As of right now, TVEC is the only approved virus used for treatment against cancer, specifically melanoma(a type of skin cancer) in the US. One of the key aspects of TVEC that makes it so promising are the deletions in the HSV-1 viral *y34.5* and *a47* genes.[11] The main function of the *y34.5* gene is to prevent the host cell from shutting off its protein synthesis.[11] By inhibiting this gene, TVEC would be unable to infect normal cells because protein synthesis is inhibited, preventing replication.[11] Cancer cells, on the other hand, do not have the ability to shut off protein synthesis, meaning TVEC can only replicate in these cells.[11] The *a47* gene normally functions to disrupt the transporter of the host cell.[11] If this gene is inhibited, then the cell would not prevent the *MHC* class 1 expression, which in turn promotes antitumor immune responses such as *MHC-1* expression (produces antigens used by T cells).[11,32] This groundbreaking advancement paves way for the potential of virotherapy to fight cancer as an effective and safe treatment. If research continues in this direction, genetic engineering promises a major victory against cancer.

With the advent of CRISPR/Cas9 genome editing this technology could be even more widespread to engineer other viruses to target cancers. The duality of cancerous cells versus healthy cells is very thin. Viruses will target cancerous cells because they are still part of the human body, making them seem like the perfect method of treatment. Also, the rapid rate of cell division within cancerous cells allows viruses to be one of the greatest tools possible. Simply put, the more cancer cells, the more host cells, which in turn allows the viruses to spread further and eradicate tumors. Furthermore, there are many viruses that target a specific cell in our body; for example, chickenpox specifically targets the skin[33], so the varicella-zoster virus may be a potential starting point in creating a virus that fights skin cancer. Even though viruses may seem like the perfect solution to cancer, its viability in the current field is limited because much further research

is required, specifically using other viruses to infect cancer cells in other organs, not just TVEC for melanoma.

Challenges and Limitations

Although promising, there are many challenges that remain with any new technology. One common difficulty that appears in most attempts to genetically modify DNA is off-targeting. Off-targeting is the phenomenon that takes place when the wrong area of the DNA is targeted by the genome editing tools, making an unwanted DNA break or genomic edit in the cell.[34] This is possible in both CRISPR and virotherapy, which is why research must focus on addressing these problems. In CRISPR and virotherapy, because DNA is so large on the micro level, there are loci in the genome that have the same or very similar DNA sequences, even if they are in or near different genes, or on different chromosomes. As a result, the guide RNA may guide the Cas-9 enzyme to the wrong site.[12] Off-targeting or unintended editing may occur at different parts of the DNA which can be harmful to the cell. If anything, this can result in damaged and mutated DNA or even worse, develop into cancer.[35] Key solutions may include culture experiments that focus on how these edited viruses work on the molecular level, both against healthy and cancerous cells to ensure that the virus is properly edited to attack cancerous cells only. These viruses should not be attempted in clinical trials unless they have been verified through experimentation to be safe and effective, which can be accomplished by exposing these viruses to a small subculture of cells, imitating a tumor in a human body. This ensures that we can test the virus on a smaller scale to avoid any dangers before testing it on an actual person.

Viruses can be dangerous to control. Because of their natural rapid replication rate, viruses are more prone to mutations. This means that even if we are able to perfectly modify a virus, there is still a chance for it to mutate and reverse the modification or develop new, unexpected mutations, potentially resulting in uncharacterized impacts on the cell and body.[36,37] In order to avoid this, development of replication-incompetent viruses in the lab for treatment purposes may be useful in testing out the effects of certain viruses on different tumors.[38] The effectiveness of these treatment options will also be impacted because modifying the genetic material of either a cell or virus results in a less fit version. Even with viruses that cannot replicate, there are limitations. For example, the amount of viruses that would be engineered may vary from patient to patient. These viruses should be able to help the goal of using a virus to fight cancer because it resolves the potential of mutations as well as the rapid spread of viruses that would normally occur in a human body, and instead, keep these viruses near the target site. This can be resolved through multiple rounds of treatment, so medical professionals can monitor the effects a certain number of these viruses have on the tumor, which would gauge us on how many viruses may need to be engineered. One last detail that must be resolved is whether the replication-incompetent viruses will be able to kill cancerous cells. This is because viruses tend to kill cells by taking over the host and producing copies of itself. In other words, as far as we know, viruses cause programmed cell death in order to further spread itself through the body, but if it cannot replicate itself and cannot spread, the question still remains, will it complete its purpose which is to kill the cancerous cell? This key question can and will only be answered through numerous experiments

with these non-replicating viruses and their effects on any cell. In comparison to cancer cells which have rapid growth, most cells with edited genomes cannot compete because they replicate slower, hence they are less fit.[21] Perhaps this means that the cells will not survive as long as the cancer cells, but perhaps they will survive long enough to target the cancerous tissue and start fighting. A clinician may be able to answer this question after various trials on the efficacy of cells with edited genomes.

Application of genome editing remains a challenge in cancer as well. Cancer is an extremely broad category, consisting of multiple different types and within each type, each cancer can be caused by multiple different mutations.[39] Because of the wide range of types of cancer and the variety that can be found in patients, each patient requires an individual assessment of the cancer, as different treatments or combinations may be required. Because of this, there is no one solution that can finally cure cancer, which is why these challenges and limitations must continue to be researched. TVEC, the only FDA approved form of virotherapy, has been successfully implemented as a form of treatment specifically for melanoma. However, like most drugs, TVEC has many side effects and downsides. TVEC is a herpes virus, which can cause symptoms such as rashes, inflammation from cell death, infections, hypoxia, fatigue, fever, and other flu like symptoms which were all observed in Neoadjuvant Intralesional Injection of Talimogene Laherparepvec With Concurrent Preoperative Radiation in Patients With Locally Advanced Soft Tissue Sarcomas, a study conducted by the University of Iowa and completed June of 2023.[40] We cannot control TVEC because of the way it was engineered. For example, TVEC can target healthy cells, and when TVEC targets a healthy cell, the cell will kill itself, preventing the spread of the virus.[11] Better specificity will be required if we wish to safely and efficiently use TVEC to fight cancer.

Potential future directions

Many potential treatments using oncolytic virotherapy and genetic engineering against cancer are not ready for clinical trials and require further research. Most of the methods discussed in this paper focus on theoretical approaches towards usage of CRISPR in the cancer field. We do not fully understand how to effectively avoid off-targeting in the case of both virotherapy and genome editing. Therefore, off-targeting effects need to be studied in order to better understand both their clinical and molecular impact, to mitigate those effects, and in order to minimize or eliminate off-targeting of genome editing tools in disease. Off-targeting can be deterred by ensuring that the guide RNA is one-of-a-kind, in other words, the sequence in the gRNA is not repeated anywhere else besides the site of target, and there are some desired cut sites where this would not be possible due to similarity of sequences in different parts of the genome This can only be resolved through trial and error and continued efforts of ensuring the safety and application of CRISPR.

Even if we eliminate off-targeting of genome editing, there are potential side effects of virotherapy approaches, which can still be harmful or unpleasant for a patient. These problems can be mitigated by using a fabricated colony of both healthy and cancerous cells to test out the accuracy of virotherapy. For example, even though TVEC is only approved for melanoma[31], it is

created to only reproduce in cancer cells, which can result in unknown side effects. Figuring out the effects of these excess viruses should remain a priority to mitigate side effects and ensure patient safety and comfort. Therefore, more clinical trials will be needed in order to understand those side effects and honestly convey them to patients and providers, and the results of these trials can then be used to inform pharmaceutical research in order to modify the treatment to minimize impact and risk of these side effects.

Effectiveness of the edited cells against cancer itself remains an open question in the field. Before these drugs become widely available and a common treatment against cancer, researchers must test and validate that they can effectively target and fight the cancer. Before entering into clinical trials, the most common mutations will need to be studied in the lab with this treatment, using cellular systems and animal models prior to clinical trial in order to ensure effectiveness and safety against the cancer. These experiments could expose cultured cancer cells to replication-incompetent viruses that are known to infect that particular cell type. For example, they could focus on several different cancer cell lines derived from liver cancer. The researchers could infect the panel of liver cancer cell lines with a panel of several different viruses, replication-incompetent versions of the viruses, and genetically modified versions of the viruses that, similar to TVEC[31], make the virus safer by making it less likely to spread. The control would be each cell line growing without exposure to any virus, which will serve as a comparison for the cancer cell growth under non-treatment conditions. The team of researchers could then perform cell growth and cell division/cell state assays to assess how the cancer cell lines respond to each condition, and could perform experiments on the molecular responses in the cell types to each virus to better understand the mechanism of the response. For example, if all of the cell lines respond well to one of the conditions by showing decreased growth and cell cycle arrest, this might be a great candidate for further study. Then, the mechanistic study can give insight into how the virus is influencing cell health and could also help with understanding how a patient's body may respond to the treatment. The same procedure would be used later on in a mouse experiment, once a few treatment options are validated and approved in cell lines and the molecular mechanism behind the virus is adequately investigated to be safe and effective. That way, testing can move beyond a culture of cells and onto multicellular organisms, like mice to assess safety and side effects in an organismal setting. Similar steps would be repeated in this experiment, but the main difference would be the focus on how the virus affects the organism as a whole. The large hurdle in this step of trials would be to create a sufficient number of test subjects, in this case, use mice with different stages of liver cancer and make sure there are multiple at each stage to study. The experiment would consist of four control groups, where the mice will have liver cancer from stages 1-4. In these groups, the mice would live unexposed to the virus, while the experimental group would be exposed to different quantities of the virus. There would be four experimental groups as well, which will be organized based on the stage of liver cancer the mice are at. Each mouse would be exposed to different quantities of the virus to gauge the effectiveness of non-replicating viruses in a controlled environment. The key of this experiment is not only to further discover if the virus is effective in an organism, but to find the most efficient treatment

method of the virus within the different stages of liver cancer and to see how the exposure to a foreign virus would affect the organism as a whole. The main question researchers should look at is how does the body react to the virus and will they bypass the immune system or will the immune system fight them off before they can kill the cancerous cells. Even though we are injecting viruses that should not attack healthy cells, they are still considered pathogens and foreign to our body, which must be understood before moving beyond these trials. The next question would be to determine whether the cancer comes back. Once these questions are answered, the most effective methods will be later used on larger organisms, and eventually on humans once they are deemed safe and effective for human trials.

In a hospital and clinic setting, each cancer is unique and has different mutations and affects different cell types, which means treatment will require a controlled environment for personalized treatment where the team of providers and researchers work together to develop a treatment plan based on the patient's specific case, clinical presentation, and mutations. This controlled environment and personalized approach to medicine will help us learn about cancer more broadly and how it interacts with our cells. Studying the mutations that are observed in the clinic and for which this treatment is likely effective will help us better understand genetics and healthy versus cancerous states of cellular behavior. Although promising, cancer remains one of the deadliest diseases and will most likely continue even after perfecting virotherapy. Each cancer case will vary and require consistent monitoring and continued use of current cancer treatments, such as chemotherapy or transplants to completely remove the cancer, may be required in coordination with emerging virotherapy treatments. Because each treatment may vary in effectiveness depending on the patient, virotherapy promises a new approach and option in fighting cancer. The field of study has not discovered exactly how the CRISPR/Cas9 system would function within a human body, but recent advancements have shown promising potential, specifically through the editing of mammalian cells.[41] Another key focus that remains undiscovered is how CRISPR may affect humans long term. For example, chemotherapy tends to harm people, especially children because it stops cells from dividing.[42] Even within adults, chemotherapy causes other problems such as fertility because of the reduced cell division. Therefore, it is safe to assume that CRISPR may result in similar or other long term problems that need to be discovered and understood before it can be considered a safe option for cancer. Even though CRISPR is known for its precision, unlike chemotherapy, researchers are not aware of the potential within the macro level of the human body. Such research is pivotal before the advancement and continued discovery of this new life saving technology.

Conclusion and Discussion

We have described that CRISPR/Cas9 genome editing has had a major impact on research advances, medical possibilities, and will continue to have a major impact in the clinical world. Oncolytic virotherapy, or the co-opting of viruses to fight cancer, is another cutting-edge advancement in cancer research. Genome editing paired with oncolytic virotherapy, have the potential to help improve quality of life and clinical outcomes for those suffering from cancer. The application of CRISPR shows great promise in fighting cancer. Through editing the viral

genome, virotherapy becomes a viable treatment option because of its ability to avoid side effects present in other treatment options, such as chemotherapy. Utilization of CRISPR on viruses will likely bring virotherapy to the frontline of the battle against cancer.

The field is heading towards a promising future, but research must continue in order to achieve this dream. The main challenge remains in improving the effectiveness of virotherapy and how they can be safely administered to patients. Continued research and clinical trials will be required in order to ensure that virotherapy can efficiently fight cancer. Currently, even when cancer is fought off, it can reemerge as a result of leftover cancer cells or cancer-causing mutations. Virotherapy has the potential for complete eradication of cancer cells because the virus will seek to replicate in all cancer cells, eventually killing them all. Gene-targeted therapy with CRISPR has promise to target and fix the mutations that have already occurred, which can prevent future cases of cancer. The combination of the two will only increase the efficacy of virotherapy and create safer treatment options for cancer patients and ensure that the cancer does not return.

Once CRISPR and virotherapy have effectively been integrated together and implemented into cancer treatment, its utilization and potential exists in other areas of health. Genetic engineering doesn't have to stop at cancer. It can help us fight other diseases and revolutionize the clinical field to improve human health. This isn't about winning the battle, it's about winning the war.

Acknowledgements

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The Effect of Music on Postoperative Pain and Anxiety By Nethra Pai

Abstract

Patients often experience various negative effects of surgery including postoperative pain and anxiety at moderate, severe, or extreme pain levels. Additionally, many patients experience postoperative anxiety which may increase the duration of hospital stay. The most commonly applied solution, opioid analgesic medication, has increased rates of morbidity and mortality, necessitating research into non-pharmacologic alternatives. Because music is universally accessible, affordable, and non-addictive, it is a promising supplement to traditional pain management options. The aim of this review is to explore the impacts of music on postoperative pain and anxiety and determine whether it can be used to effectively treat patients. In this review, music showed various levels of efficacy for pain and anxiety but showed that the use of opioid analgesic medication and s-cortisol levels were reduced. Almost all studies showed that patients felt the music helped with symptoms. This review concludes that music should be utilized as a tool to mitigate the various after-effects of surgery, even if not always with significant differences, as it is low-cost, accessible, non-addictive, and ultimately provides positive effects.

Introduction

Approximately 468 million surgical operations are performed every year [1]. Surgery is often the only method to treat certain ailments, but patients often experience various negative effects, including postoperative pain [2]. According to the US Institute of Medicine, 80% of patients who undergo surgery report postoperative pain, and 88% of patients with postoperative pain also report moderate, severe, or extreme pain levels [3]. If managed inadequately, postoperative pain can prolong recovery, increase hospital stay, increase healthcare costs, and reduce patient satisfaction [4]. Opioid analgesic therapy has served as the mainstay of treatment for acute postoperative pain. However, as opioid misuse causes increased rates of morbidity and mortality, investigation into alternative pain treatment strategies is rising [5]. Nonpharmacologic treatments are recognized as strong adjuvants to pharmacologic treatments, such as opioid analgesic therapy, being valuable, simple, and inexpensive [6].

Additionally, many patients experience postoperative anxiety due to fears of pain, surgical failure, death, and loss of physical functioning [7]. There is exploratory research connecting postoperative anxiety and the duration of hospital stay, where patients with high postoperative anxiety experience longer hospitalization periods and report more postoperative pain [8]. However, postoperative anxiety remains largely untreated, likely because of the lack of treatment options.

Music is almost universally accessible in today's world, making it a promising supplement to traditional treatment strategies. Music is known to have significant psychological effects, such as causing the release of neurotransmitters and hormones, and occasionally altering brain structure [9]. However, conclusions regarding the effect on postoperative pain and anxiety are

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minimal. The aim of his paper is to explore the impacts of music on postoperative pain and anxiety and determine whether it can be used to effectively treat patients.

Methodology and Results

       I.   **Methods**

      This review analyzed 9 different studies, found through Google Scholar and the NIH National Library of Medicine, to determine whether music had a significant effect on postoperative pain, anxiety, and other related factors. Articles that were included primarily did not have a paywall and were all randomized controlled trials.

       II.   **Results**

Study Analysis

Studies	Results			
	Sample Size	Surgery Type	Measurement	Significance (Y/N)
Dong et al. 2023 [10]	Total: 86 patients 43 intervention, 43 control	Cardiac Valve Replacement	Pain: Visual Analogue Scale (VAS) Anxiety: State-Trait Anxiety Inventory (STAI)	Pain: N Anxiety: Y
Allred et al. 2010 [11]	Total: 56 patients, 28 intervention, 28 control	Total Knee Arthroplasty	Pain: McGill Pain Questionnaire-Short Form (MPQ-SF), VAS Anxiety: VAS	N
Lin et al. 2020 [12]	Total: 86 patients, 43 intervention, 43 control	Mechanical Valve Replacement	Pain: MPQ-SF	Y

Nilsson 2009 [13]	Total: 58 patients, 28 intervention, 30 control	Coronary Artery Bypass Graft	Pain: Numerical Rating Scale (NRS) Anxiety: NRS S-cortisol: mmol/L	N
Hill et al. 2020 [14]	Total: 92 patients, 46 intervention, 46 control	Native tissue vaginal vault suppression	Pain: VAS	N
Good et al. 2005 [15]	Total: 167 patients, 43 relaxation, 49 music, 37 combination, 38 control	Intestinal Surgery	Pain: VAS	Y
McCaffrey 2006 [16]	Total: 124 patients, 62 intervention, 62 control	Hip and Knee	Pain: NRS	Y
Laframboise-Otto et al. 2021 [17]	Total: 47 patients, 24 intervention, 23 control	Arthroplasty	Pain: NRS, equianalgesic opioid doses	Y
Nilsson et al. 2005 [18]	Total: 75 patients, 25 intraoperative music, 25 postoperative music, 25 control	Open Lichtenstein inguinal hernia repair surgery	Pain: NRS, Total amount of Morphine (mg) Anxiety: NRS S-Cortisol: mmol/L	Y

Fig.1: The table above is a summary of each study, including the sample size, type of surgery, measurement tools, and whether the study found a statistically significant difference.

Study Designs

Studies	Design

Dong et al. 2023 [10]	The intervention group was administered 3 morning sessions with 15 min of music therapy of binaural headphone delivery, lying in a recumbent position after a 30-minute rest. The control group received the same treatment with headphones without any music.
Allred et al. 2010 [11]	The intervention group listened with headphones to a compact disc of easy-listening music for 20 minutes before the first ambulation and for a 20-minute rest period after the ambulation. The control group had a 20-minute quiet rest period instead.
Lin et al. 2020 [12]	The intervention group rested in bed in a comfortable position and were provided several different types of soft, soothing music for patients to choose from. They listened to music via speakers or headphones for 30 minutes every night. The control group chose a quiet room and had 30 minutes of quiet rest time between 8 and 10 pm every night.
Nilsson 2009 [13]	The intervention group rested in supine position, with the bed head at 20 to 30 degrees. Music was in the easy listening category, at 60-80 bpm, and was distributed through a music pillow connected to an MP3 player during the rest.
Hill et al. 2020 [14]	The intervention group had a landscape image mounted to the wall and access to a speaker with preprogrammed music selections. Patients listened to preferred music for at least 2 30-minute sessions postoperatively. The control group had a standard hospital room, without music or landscape.
Good et al. 2005 [15]	The intervention groups received sixty-minute tapes with lightweight foam earphones and a small tape recorder. The relaxation group received tapes with 1-minute relaxation technique was repeated at 1-minute intervals. The music group received a tape with selections of the chosen type of music (out of 5 soothing genres), played continuously.
McCaffrey 2006 [16]	The intervention group had a bedside compact disc (CD) player that would automatically play the compact disc for 1 hour 4 times daily with patient selected music while awakening. The control group received standard postoperative care.
Laframboise-Otto et al. 2021 [17]	The intervention group listened to music of their choice via internet radio with the personal device they brought to the hospital for 30 minutes, once during the evening post-surgery and three times a day on postoperative days 1 and 2.
Nilsson et al. 2005 [18]	The postoperative intervention group listened to new-age synthesizer music with a 43-minute play time. The headphones used allowed conversation between the patient and the medical staff. Patients in the postoperative music

	group were exposed to a sham CD player intraoperatively and music postoperatively.

Fig. 2: The table above describes the design of each study reviewed.

Discussion

As surgery is often the only treatment available for medical issues [2], the pain and anxiety associated with these interventions represent a significant medical challenge. Opioid analgesic therapy, the primary treatment for postoperative pain, has high rates of misuse and adverse side effects. Thus, other alternatives, such as music therapy or comedy movies, are rising as potential treatments. Postoperative anxiety also remains a common but largely untreated product of surgery due to its high risk. Music is an attractive potential treatment for this anxiety and additional stress due to its psychological effects and accessibility. However, results on its effectiveness are mixed.

I.   Pain

All 9 studies used different methods to test the effect of music on pain. Different volumes, intervals of listening to music, and selection methods for music were utilized, but many studies had similar results. In addition, many studies used similar scales to assess pain, such as the Visual Analog Scale, in which a 100 mm line is labeled for the most and least severe pain and marked by the patients. Using measurements such as VAS, Dong et al. 2023, Allred et al. 2010, Nilsson 2009, and Hill et al. 2020 concluded that there were no statistically significant differences between the experimental postoperative music intervention groups and the control groups [10, 11, 13]. A potential reason for these results is the measurement method (VAS). The first 3 studies also use the same control group, which is a scheduled rest period instead of standard post-operation procedures [10, 11, 13]. Good et al. 2005 demonstrates the difference between the 3 categories, as it includes music, scheduled rest, and control groups. It also concluded that while there was a significant difference reported between music and rest groups over the control group, there was also virtually no difference between the results of the music group and rest group [15]. McCaffrey 2006 and Nilsson et al. 2005 describe the opposite, where pain showed a substantial decrease on the scale [16, 18]. Due to the potential impact of scheduled rest, it is impossible to know how much of this decrease is the effect of music, as these studies used standard post-operative procedures as a control group. Importantly, Dong et al. 2023, Good et al. 2005, and Hill et al. 2020 reported that >80% of patients felt the music helped with pain or were satisfied with care, even if there were no statistically significant differences [10, 14, 15]. The music was potentially used as a form of entertainment or even distraction from the pain, allowing the patient to focus on a sensation other than pain.

II.   Opioid Analgesic Medication

The administration of opioids and other analgesic medication is an important method of managing the pain of post-operative surgery. However, increased use of opioids potentially causes

dependency, induces side effects, and may lengthen hospital stay and duration of treatment [19]. Therefore, non-pharmacologic alternatives for pain treatment are important to potentially reduce the amount of medication necessary to treat a patient. Nilsson et al. 2005 analyzed the usage of Patient Controlled Analgesia (PCA) pumps and found that the music intervention groups all concluded with significantly lower doses and usage of the drugs [18]. Allred et al. 2010 also measured the usage of PCA pumps as well as requests for oral medication but found that there was little to no difference between the experimental and control groups [11]. On the contrary, Laframboise-Otto et al. 2021 utilized standardized equianalgesic opioid doses but also found that there were no statistically significant decreases [17]. This difference is likely due to the difference in control groups, as well as the procedure for implementing music therapy in Nilsson et al. 2005. Laframboise-Otto et al. 2021 also utilizes anesthetic nerve blocks, which likely impacted the overall usage of opioids. Patients in Allread et al. 2010 and Nilsson et al. 2005 reported feeling far less pain despite lower usage of analgesics, which means that the pain must be substantially reduced [18]. This makes music a potential alternative or supplement to previous pharmacological treatment options for pain, although additional research must be completed.

III.   Anxiety

Post-operative anxiety is also associated with higher post-operative pain [20]. Dong et al. 2023 and Nilsson et al. 2005 reported a significantly lower anxiety score for their patients [10, 18]. In contrast, Allread et al. 2010 and Nilsson 2009 reported no significant difference between the control and experimental groups, and music did not affect patient pain or anxiety levels [11, 13]. There was no uniformity in the results of these studies. While the measurements do not show concrete results, more research with larger sample sizes and stronger covariate control is necessary, as many studies found additional reasons for potential anxiety and pain reduction. For example, Laframboise-Otto et al 2021 also included the effects of paintings within the patient's room, and multiple studies varied control groups between scheduled rest and standard hospital procedures [17].

IV.   S-Cortisol

Extreme amounts of stress have detrimental impacts on health, adversely affecting the immune, cardiovascular, neuroendocrine, and central nervous systems [21]. Specifically, these effects could cause damaging side effects and complications, hindering recovery and increasing hospital stay. Post-operatively, a majority of stress for patients is the potential for extreme complications. S-cortisol has long been used as a biomarker for stress as it is produced in the adrenal gland in response to stress [22]. Therefore, if music can reduce s-cortisol levels for a patient, it may also reduce hospital stay and shorten recovery. While only Nilsson et al. 2005 and Nilsson 2009 measured s-cortisol levels postoperatively, the results are promising. Nilsson 2009 found that the music group significantly decreased s-cortisol levels for patients, which correlates to a decrease in stress [13]. Nilsson et al. 2005 found that while all 3 groups (intraoperative music,

postoperative music, and control) fluctuated, therefore having no significant difference, the postoperative music group had a larger decrease in s-cortisol levels within the first 2 hours of measurement [18]. These results may arise from numerous reasons, such as the surgery type. Although the effect may be small, music may be increasingly important as there are few ways to reduce stress currently.

V. Gaps and Limitations

Almost all of the research in this field uses very similar types of music, often with no patient choice. This music is designed to have a calming effect, generally being 60-80 bpm and without lyrics. While all patients liked the music provided, additional research into patient-preferred genres of music should be done as it may have different results. A patient's favorite music genre may impact its effect since familiar music may be more calming. Previous studies also find that different races or cultures may have varying pain sensitivities based on the stimuli [23]. However, the research used in this paper is varied across different continents and surgeries so it is difficult to draw conclusions based on regional and biological factors, such as race, sex, and geographic area. Finally, more research should be done comparing the effects of scheduled rest to music, as it often overlapped with the results of the research but was impossible to account for.

Conclusion

Music seems to have a generally positive effect on postoperative patients of all different types of surgery. While less effective in certain areas or surgery, it still distracts patients and redirects their attention so that they perceive less pain and are less stressed. The effect of music on S-cortisol levels and medication use is also increasingly important. When tested, music decreased stress levels and the use of analgesics, where increased levels could be potentially detrimental to patients. However, these areas particularly are unexplored, and additional research is required to see if this is a widespread effect. There needs to be additional research into intersections of the effect of music, and other potential therapies. Ultimately, music should be implemented in postoperative care. It has little to no additional risk and cost since music is easily accessible around the world and only requires maintaining equipment. It also provides numerous potential positive effects, including mitigating symptoms such as pain and anxiety which are largely difficult to alleviate.

Acknowledgments

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A lightweight MRI-based Alzheimer's detection algorithm using machine learning By Yajat Sharma

Abstract

　　Alzheimer's Disease (AD) is a degenerative disease which causes shrinkage of the brain and eventually memory loss. AD can start many years before diagnosis, and many tests exist to detect the presence of it. The OASIS Brains Project works towards collecting useful data regarding AD patients and compiles it into databases, one of which is used for this work. This work utilizes a "lightweight" analysis of the database in order to train a machine learning model to detect the presence of AD from a specific image. The models reached an accuracy of up to 82.1% using the OASIS dataset and 95.4% using a dataset acquired from Kaggle.com. These results closely match other studies doing "heavyweight" analysis with 3D images instead of 2D. This shows that lightweight methods for detecting AD can have real clinical benefits regarding time and ease of use and overall can be very influential in the world of AD diagnosis.

Introduction

　　Alzheimer's disease (AD) is a neurodegenerative disease which causes neurons in the brain to deteriorate and eventually die. The deterioration of neurons happens mainly in the entorhinal cortex and hippocampus, causing dementia, pertaining to symptoms such as poor memory, difficulty learning, and overall ability to function. The research of this disease began in 1901 when Dr. Alois Alzheimer started working with Auguste Deter, a woman who had been experiencing symptoms such as memory loss, inexplicable changes in behavior, and problems with speaking and writing. She passed away five years later. This case is a classic example of how AD presents itself over time. It starts with simple memory loss, something often overlooked in people's everyday lives, but then moves to more severe symptoms such as affecting language, behavior, and reasoning. Over time, the disease progresses and is ultimately fatal.

　　Current estimates show that there are about 55 million people in the world who have dementia, most of whom have AD (1). There is no cure for AD, but there are treatments, both drug and non-drug, which help with symptom management. In the time after Dr. Alzheimer's research, many assessment tools were developed to monitor patients with AD and the progression of the disease over time. Clinical Dementia Rating (CDR) was first introduced in 1982 for a study of people with mild AD. CDR is calculated based on six different cognitive factors: personal care, interpersonal behavior, memory, problem solving, orientation, and performance in hobbies.

　　The CDR rating works by asking questions from both the informant and the subject. The questions for the subject include memory or problem solving. The questions for the informant ask about the subject's performance in answering their questions. As for the rating itself, it is based on a scale from 0-3. 0 corresponds to no dementia, 0.5 corresponds to questionable dementia, 1 corresponds to mild cognitive impairment (MCI), 2 corresponds to moderate cognitive impairment, and 3 corresponds to severe cognitive impairment. CDR's interrater reliability is

relatively high, displaying that it can be used to precisely predict a patient's level of impairment across multiple instances (2).

Another test is the Mini-Mental State Examination (MMSE), introduced in 1975, which is a short assessment on the cognitive abilities of hospitalized patients. Over time, it became very popular and is now considered as the most widely used test of cognitive abilities (3). The MMSE consists of two parts. The first part contains questions to evaluate orientation, memory, and attention of the patient. The second part evaluates the verbal and written abilities of the patient.

As the usage of the MMSE continued, many advantages were found. For example, it is very simple to administer and is very concise. It is also accepted internationally and can be applied to large samples of patients. On the other hand, with this test comes a few disadvantages. Some are that there are numerous versions, and that there is a lack of accommodation for cultural variances and a lack of coverage of all cognitive areas. Additionally, the MMSE does not account for patients who are hearing or visually impaired, who do not have substantial English literacy, and patients with other communicative disorders. As a result, these patients do not perform well on the MMSE despite being cognitively able (4).

One of the earlier tests for dementia was the Clock Drawing Test (CDT). It was created in the early 1900s to assess the cognitive state of soldiers who had suffered head injuries in the field. It is one of the simplest tests for dementia as the only task asked of the patient is to draw a clock. The reason for its effectiveness is because when drawing a clock, various skills which are generally affected by dementia are required. For example, following directions, understanding language, visualization, and carrying out normal movements. In patients who have taken the CDT, a positive test calls for a diagnosis of dementia. A negative, or regular test, however, is not as insightful to the patient's cognitive abilities, shown by the fact that around half of the patients with dementia taking the CDT test negative.

Another, more recent test, is the Montreal Cognitive Assessment (MOCA). It was developed in 1995 to detect MCI. The MOCA covers a few different cognitive function areas, such as, orientation, short term memory, visuospatial ability, language, abstraction, naming, ability, and even includes the CDT. Similar to the MMSE, one disadvantage to the MOCA is it does not cater to every patient's needs.

The issue at hand is that in most instances, AD goes undetected for several years before diagnosis. Across the globe, it is suspected that approximately 75% of all Alzheimer's cases go undiagnosed. This can reach up to 90% in lower income countries (5). This is caused by a few main reasons. One reason for this severe underdiagnosis is the incredibly high cost of medical imaging required to make a diagnosis. The three main imaging types used are PET, MRI, and CT scans, which each cost $10,700, $8,400, $4,800 respectively. In addition to this exceedingly high cost, lots of discomfort is involved with diagnosing AD. For many patients, spinal taps can be uncomfortable during and after the procedure. Another cause of discomfort stems from PET scans, which require patients to remain immobile for 30 to 45 minutes. These factors make an AD diagnosis simply undesirable. The third main reason is the inability to accurately diagnose AD both preemptively and even when symptoms appear. In most cases, patients are not tested for AD

until they display signs of cognitive deterioration. However, AD starts affecting the brain 10 to 20 years before symptoms appear. So, by the time AD is diagnosed and treatment starts, the disease has already done significant damage to the patient. Even after the point when patients start to exhibit symptoms of AD, it is still difficult to diagnose it.

AD causes the degeneration of neurons, which will show up on brain imaging. Despite this, brain imaging is not generally used to diagnose the condition. This is due to the fact that regular aging also causes neuron deterioration creating a level of overlap between regular aging that makes it difficult for doctors to make a definitive diagnosis .

Machine learning (ML) can solve these problems by providing systems that are both accurate and incredibly cost efficient. ML is already being used for coronary artery disease, epileptic seizures, arrhythmia, and many other medical conditions (6). In this work, I have developed a ML model to detect AD using MRI images of the transverse plane. This model was trained on the data of over 400 patients, with and without AD. My hypothesis was that my model would be over 90% accurate. My results show that the model was fairly accurate in detecting AD in these patients, with a 95.44% accuracy.

Methods–Data acquisition:

This work employs the datasets from the OASIS Brains project, specifically OASIS-1. OASIS-1 contains cross-sectional MRI data of 416 patients of ages ranging from 18 to 96 with varying severities of AD. Every subject in the dataset includes 3 or 4 T1-weighted MRI scans from a 1.5T vision scanner in a single session. Additionally, these subjects are all right-handed men and women. Of the subjects over the age of 60, 100 of them have been diagnosed with mild to moderate AD. Images from 20 nondemented subjects taken on a session within 90 days of their initial session is also included as a reliability data set.

Each subject's data includes a text file containing a summary of all their session information. The information contained in each text file is as follows: session ID, age, sex, handedness, education (EDUC), socioeconomic status (SES), CDR, MMSE, estimated total intracranial volume (eTIV), atlas scaling factor (ASF), normalized whole-brain volume (nWBV), and delay. EDUC refers to the number of years of education of the patient. SES is assessed using the Hollingshead Index of Social Position. eTIV and mWBV are used to determine certain anatomical features of the patient. Delay refers to the group of patients who were imaged in a subsequent session. Many different types of MRI images are provided in the dataset, but this work made use of images with the label of "_t88_masked_gfc_tra_90". In addition, this work only made use of the CDR as the determining assessment tool of the patients' cognitive abilities as it is the most accurate and widely used.

This work also makes use of a second dataset obtained from Kaggle.com. This dataset was compiled by Sarvesh Dubey and is perfect for this work. It contains images taken from the transverse plane and is already separated into 4 classes, "MildDemented," "VeryMildDemented," "NonDemented," and "ModerateDemeneted." It is also divided into training and testing sets, making it easier and faster to utilize. In addition to its exceptional organization, it contains many

times more images than the OASIS dataset. It contains 6400 images, as opposed to the mere 430 from OASIS. This means that the model can be even more accurate and has much more to work with.

The second dataset from the OASIS Brains project, OASIS-2, was also a viable option for this work. It contains longitudinal MRI data of 150 patients of ages ranging from 60 to 96. Like OASIS-1, these patients were scanned with a 1.5T vision scanner and were T1 weighted. Unlike OASIS-1, these patients were scanned multiple times; the sessions separated by at least 1 year. Given the number of visits versus number of patients, there were a total of 373 sessions completed for the 150 subjects. Similar to OASIS-1, OASIS-2 also includes a summary of all the patient's information in one file. Unlike OASIS-1, OASIS-2 does not provide pre-processed images. Only raw images are given, so skull removal is not readily obtainable. Because of the lack of preprocessing, this dataset was not utilized in this work as the time and difficulty of creating images to perfectly match the ones in the OASIS-1 dataset would not be worth gaining just 150 images, which would likely not have a significant effect on the performance of the model.

Method Organization:

This work was organized into 4 separate trials. The first is a trial conducted which excluded all the patients who did not have a recorded CDR in their summary file. The second trial brought all the patients without a CDR back into the classification but labeled them all as "normal" patients, meaning without any trace of AD. The third trial changed the number of classes but the number of patients remained the same. The reason for this change will be discussed ahead. The fourth trial is separate from the first 3 as it utilized the dataset obtained from Kaggle.com to do its classification, but the algorithm and processes used to train and test are more or less the same.

For the first 3 trials, training and test sets were selected at random and were filled to contain a similar amount of images per classification. For this work, only images of the transverse plane were utilized for training and testing as separate studies have shown that images of the coronal plane did not yield adequate accuracies. Other works have applied the capabilities of 3D images provided by OASIS, but for this work, lightweight classification was used. As for the image processing of the third trial, the images to be inputted into the model faced a problem. There are very few subjects who were given a CDR of 2, and many more who were given a CDR of 1. If classification were to be performed on four different classes (CDR of 0, 0.5, 1, and 2), results would be incredibly inaccurate given the underrepresentation of subjects with a CDR of 2. The workaround to this issue is to group subjects with CDR 1 and 2 together to provide for more representation of this singular group as opposed to two different ones.

Data Organization:

Dataset organization of the OASIS dataset was automated using a custom python script. In the dataset, each subject's file contains a text file within it. Listed in this text file is an informative

summary about the subject's information. As stated previously, the information contained is: session ID, age, sex, handedness, EDUC, SES, CDR, MMSE, eTIV, ASF, and nWBV. For this work, only the CDR was used to categorize the subjects into their respective severities of AD. The script functions as follows: first, it traverses through the source folders while constructing the path to the text file. Then it searches for the CDR within the file. The files are then assigned a set image type depending on the CDR value. A 0 corresponds to "normal," 0.5 corresponds to "mild," and 1 and 2 both correspond to "severe." A factor which became very apparent following manual examination of the files is that some subjects simply did not receive a CDR value which posed a great issue. No classification can be done if an image has not been previously classified. The workaround to this was to disregard the subjects without a CDR, skipping them entirely for the first trial. Though acting as a solution, this may be the cause of a lower accuracy due to less representation of classes overall, which is why the subjects without a CDR were put back into place for the second and third trials. Once the image type is set, the path to the image itself is constructed. Following this, the image is transported to a destination folder depending on its image type.

The first trial, as stated previously, required the removal of all data points which did not include a CDR. This greatly diminished the amount of usable data, reducing it from around 400, to just 191. It is not safe to assume that all of these data points were all part of a single class. In order to determine which class (if from a single class) these data points were from, tests were conducted. The second trial was conducted to see if reincorporating the patients without a CDR back into the data as "normal" patients would have any effect on the accuracy of the model. If the accuracy increased, that means that these patients indeed were "normal." If it decreased, then it means that they are all part of a different class, or are from completely different classes altogether. The third trial was conducted in order to see if combining the less represented class into a larger class would improve accuracy of the model as it would have more data for each class to work with. This trial was conducted when the number of "Severe" patients in the training and testing data was much lower as compared to the other two classes. Thus, "Severe" and "Normal" were combined. The fourth trial was conducted to see if the same processes but a more detailed dataset could yield a higher accuracy. This was very probable as the dataset utilized in this trial contains about 16 times more data than the OASIS dataset used in the previous 3 trials. More data points for a model to work with generally correlates to a higher accuracy.

Algorithm description:

In this work, classification is performed on various MRI images to determine the subject's level of AD. The algorithm family used for this classification in the first trial is the ResNet family, specifically ResNet50. ResNet is a convolutional neural network (CNN) and is best used to analyze images, making it perfect for image classification. A regular neural network is a system

which takes inputs, performs calculations on those inputs, and returns an output.
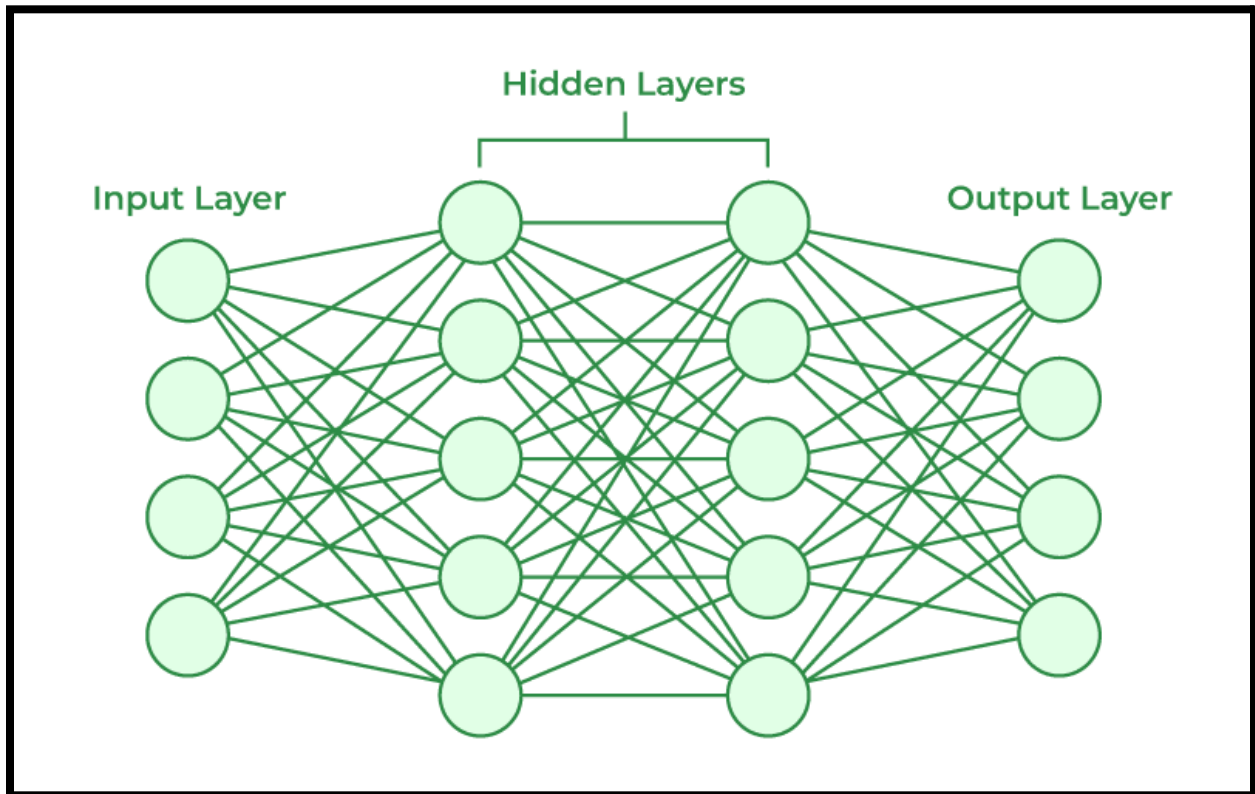
As displayed in the figure above, a neural network's input nodes are all connected to the next layer, called the hidden layer. These connections are called neurons. Each input node is connected to each node of the next layer, and each node of that layer is connected to each node of the next layer, and so on until the output layer is reached. CNNs are different from traditional neural networks because they treat the data being fed as spatial. Instead of each node of each layer being connected to each node of the next layer, they are connected to the nodes closest to them, making the whole process much easier. In addition, they include extra layers, the most important being the convolutional layer where a "filter" is put on top of the image and a feature map is created, making it perfect for working with images. CNN: The algorithm used for the next 3 trials was VGG-16:
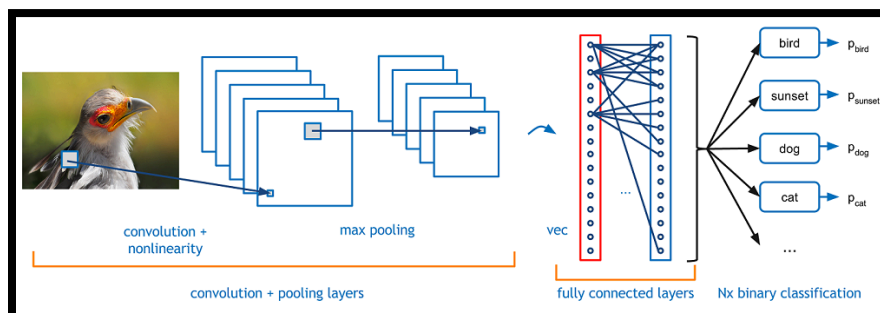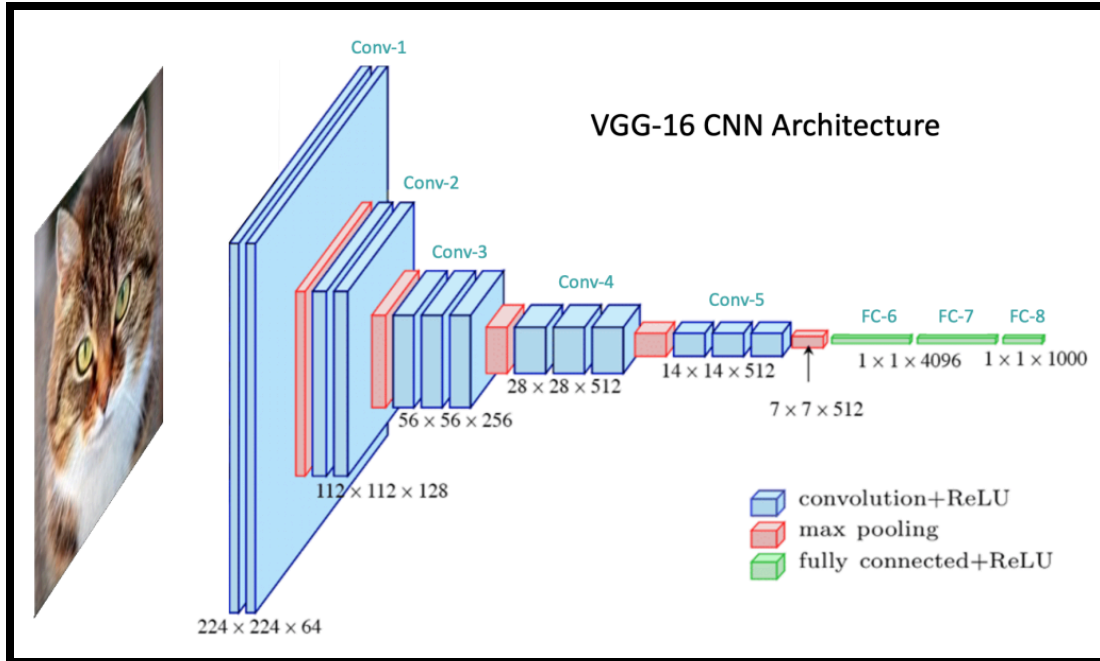
Training/Testing procedure

     While training the model, a set procedure was followed for all 3 trials. The first step was to initialize the model. It was initialized using the ImageDataLoaders function, rather than the more popular, but deprecated, ImageDataBunch. Then, the model is trained on a few epochs and a preliminary accuracy check is conducted by generating a confusion matrix. Then, the optimal learning rate is found by using a loss vs learning rate graph:
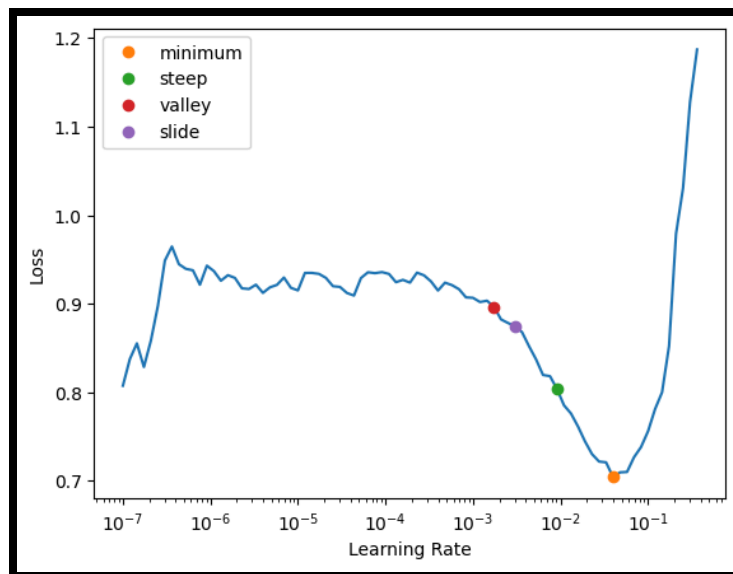
Following this is another set of training a few epochs. The alternating cycle of determining the optimal learning rate and training a few epochs continues until a sufficient accuracy is obtained. Finally, the accuracy of the model is calculated in 2 different ways to ensure consistency.

One thing that can happen when training a machine learning model is a very low initial accuracy, which is exactly what happened for every trial. Despite the low starting accuracy, accuracy of all four models increased over time as training and revision of the learning rate went on. For example, in just the first five epochs, the model of the fourth trial improved from 55.9% to 70.1% as seen in the figure :

epoch	train_loss	valid_loss	accuracy	time
0	1.902646	1.197890	0.558801	00:51
1	1.395543	0.914107	0.651869	00:44
2	0.969984	0.779186	0.687695	00:45
3	0.756066	0.742140	0.701324	00:45

A confusion matrix is a very useful visual representation of what a model gets right and wrong and is perfectly suited for classification problems. In addition, they can be used to track a model's progress as training continues, as was done in each of the four trials. On the X axis are the predicted classes and the Y axis contains the actual classes. The boxes at which the predicted and actual classes are both the same represent a correct classification by the model. The preliminary confusion matrix of trial 4 is shown in the figure:
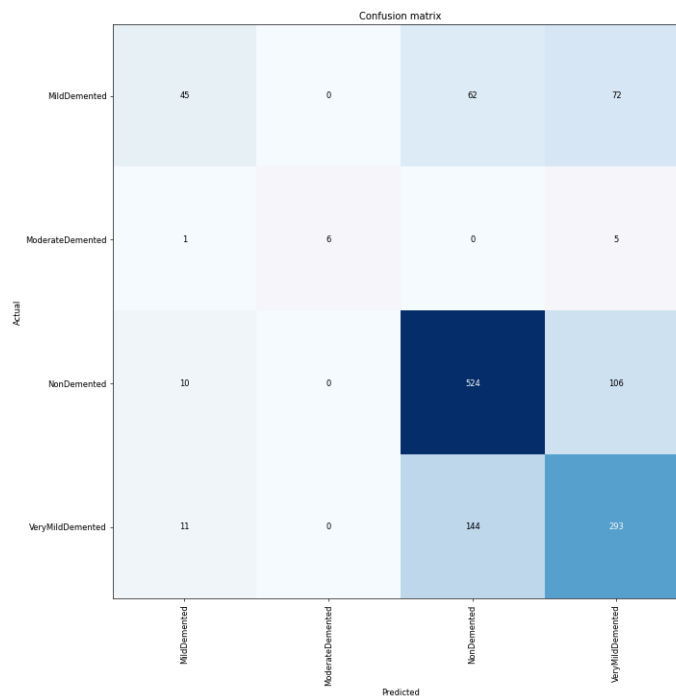
Confusion matrix

In this confusion matrix, the box containing the number 524 represents the 524 correct classifications of "NonDemented" the model made. The boxes in which the classification from the x axis does not match the classification from the y axis represent an incorrect classification from the model. A more accurate model will have a diagonal line of dark blue boxes going from the top left to the bottom right. The reason this line is not fully connected in the confusion matrix above is because the "ModerateDemented" class simply had less patients to classify for.

Results

The main metric utilized to determine the model's success is accuracy. The highest recorded accuracy from the model in the first trial (excluding non-CDR patients) is about 82.11%. Shown below is the progression of the accuracy over time:

epoch	train_loss	valid_loss	accuracy	time
0	2.021080	0.895305	0.810526	00:02
1	1.894094	0.858194	0.789474	00:02
2	1.586300	0.875602	0.768421	00:02
3	1.373103	0.860116	0.768421	00:02
4	1.219475	0.865321	0.757895	00:03

epoch	train_loss	valid_loss	accuracy	time
0	0.543013	0.756840	0.768421	00:04
1	0.504983	0.713467	0.821053	00:02

Displayed below is a confusion matrix for the model after the first training session:
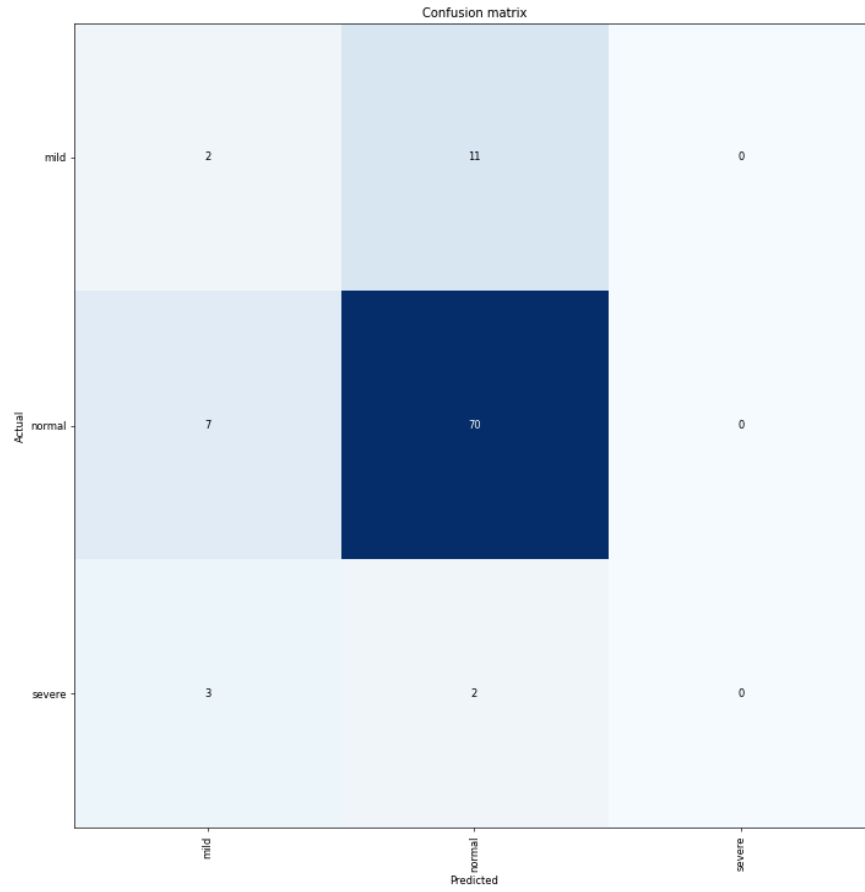
Confusion matrix

Displayed below is a confusion matrix for the model after the final training session:
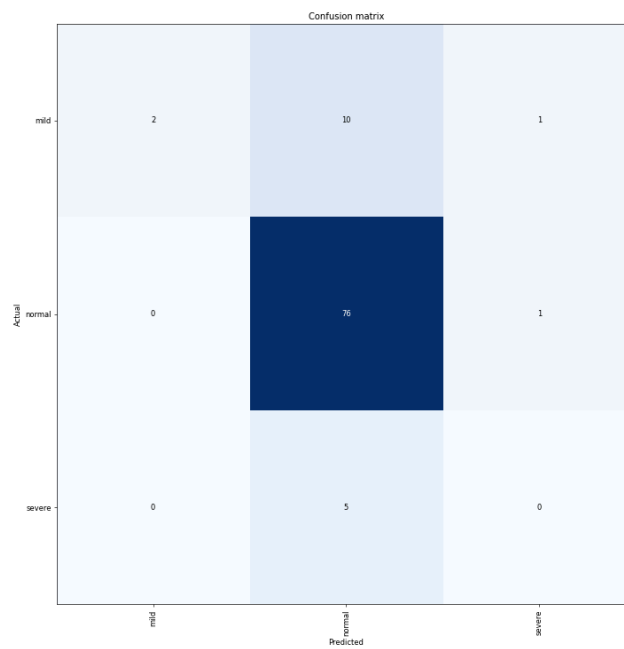
Confusion matrix

The final accuracy of the model in the second trial (including non-CDR patients) is very similar, at 82.56%. Displayed below is the confusion matrix after the first training:
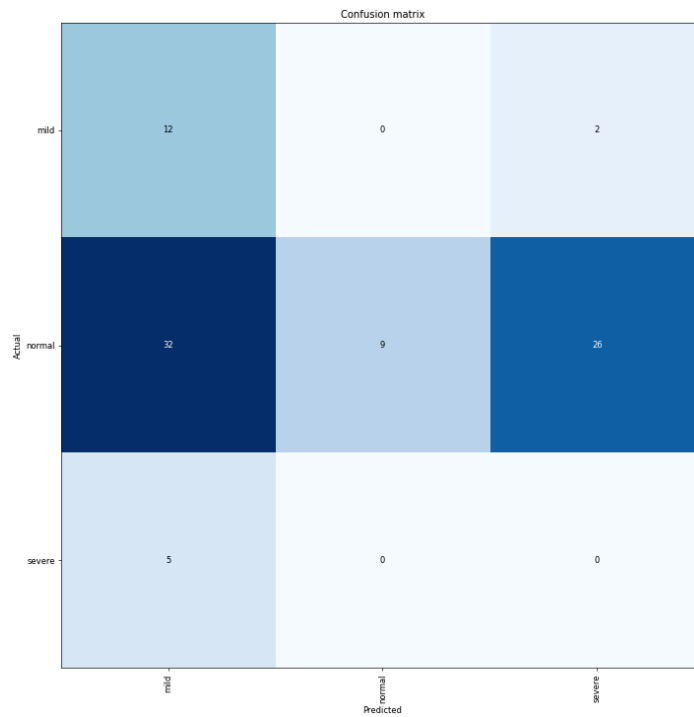
As the model progressed and became much more accurate, the confusion matrix changed as Follows:
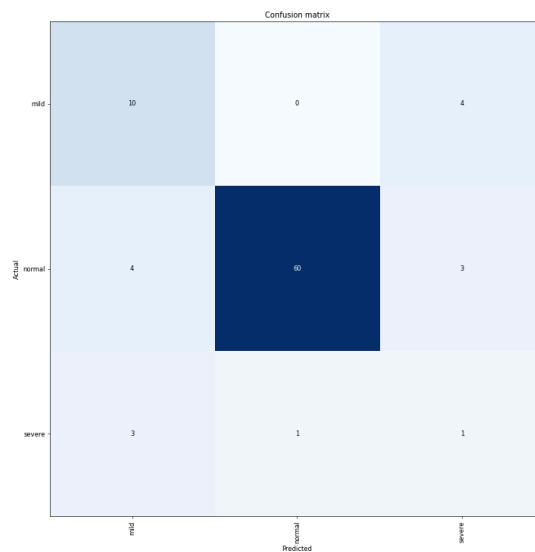
The final accuracy of the model in the third trial (including non-CDR patients with 2 classes) was exactly the same as the model in the second trial, at 82.56%. Below is the confusion matrix after the first training, where the model is already quite accurate:

The final accuracy of the fourth trial (larger dataset) was much higher than the previous trials, at 95.44%:

epoch	train_loss	valid_loss	accuracy	time
0	1.086026	1.673427	0.508956	00:57
1	0.794304	1.654527	0.556854	00:56
2	0.367613	0.217880	0.924065	00:57
3	0.146284	0.142998	0.954439	00:57

Discussion

Multiple studies in the past have conducted similar research; detecting Alzheimer's disease using machine learning. These studies have achieved similar results as well, with high accuracies. The difference, though, is that these studies utilized only 3D data to perform their classification. Though using 3D data may lead to some improvements in accuracy, the benefits are easily outweighed by the computing power and time required to process such data. 3D data is much "heavier" compared to 2D data. 3D images have length, width, and a depth, as opposed to 2D with just length and width. This means that when processing 3D images for classification, the model has to work with an entire extra dimension. This causes unnecessary time delays which can have adverse effects in the real world. As soon as a diagnosis can be made and the patient can be treated, the better. This time delay is not worth the wait also because not all the 3D data will even be useful. 3D space in the image will be taken up by the skull of the patient and processing the 3D image to remove this is not as simple as with a 2D image, where a simple crop of the image works perfectly. 2D images simply work much better for this work because they are "lightweight" and much easier to work with. The model can process 2D images much quicker as compared to 3D images, meaning that the model can be altered or revised very quickly even when in clinical usage. In addition, the accuracy of the models made with 2D images is not lower than that of models made with 3D images by a significant amount, reinforcing the benefits of lightweight models in real-life work.

Much was learned about the models of each trial through this work. The four different trials were conducted to compare: less data vs more data, more data with 3 classes vs more data with 2 classes, and having much more data overall. A comparison between the accuracies of the first and second trials shows that the removal or reconstitution of the patients lacking a CDR did not have a significant effect. Despite the shift in number of data points, the model performed

relatively the same. A comparison between the accuracies of the second and third trials shows that the combination of patients with severe and mild AD did not have any adverse effects on the model. Though it did not improve the accuracy, it did make the model slightly faster, as it only has 2 classes to deal with. When comparing the fourth trial to the others, it becomes apparent that simply having more data can be the difference between having a good model, and a close-to-perfect model. This indicates that in a real world scenario, all 4 models would perform well when provided an abundance of data. In the first three trials, the models were essentially bottle-capped by the number of data which hindered their performance. The fourth trial had many times more data and so it performed much better.

Interpretation of the models is also a way to understand how to better treat AD. If a medical professional knows that a model is consistently analyzing a certain area, it might indicate to them that the problem might stem from that area, providing the possibility for a more thorough diagnosis. Along with clinical usage, the understanding of what a model is "seeing" can aid in improving the model itself by removing parts of the images which are not "interesting" to the model. This would cause the model to work faster and possibly more efficiently. Below is a visual representation of what the model in the fourth trial might be analyzing when classifying the data provided (7):
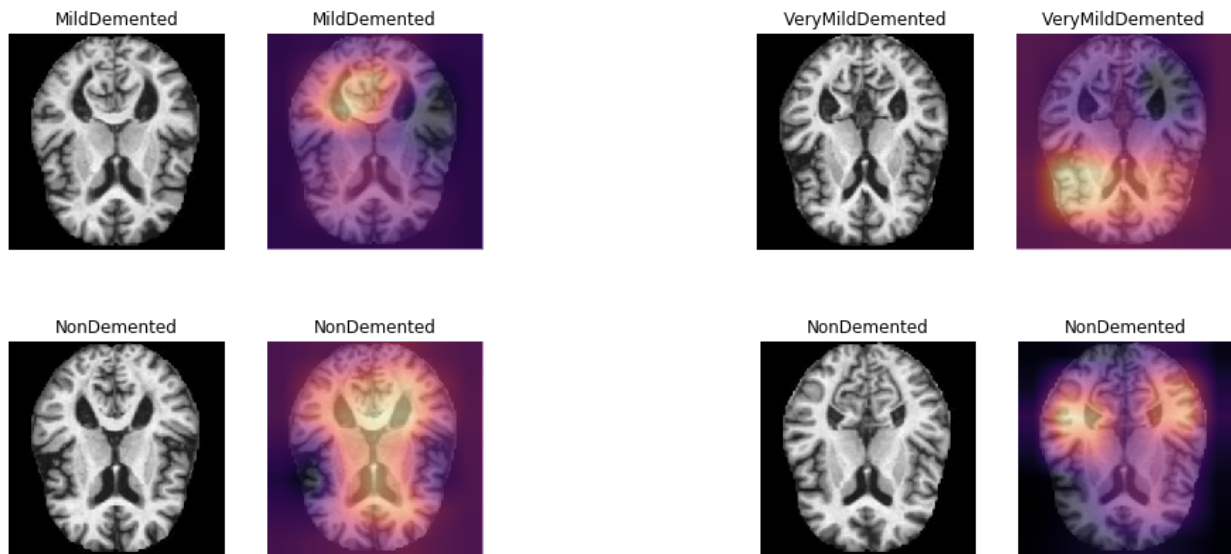
The areas highlighted in a warmer color is of "interest" to the model and is what it used to classify the image.

Future work on this topic may include using multiple classes to indicate different stages of AD, instead of different levels in different patients. It may also include simply using more datasets incorporated with OASIS-1 in order to remove the bottleneck and provide a more accurate analysis of the images. Future work may even include making the models even more lightweight to allow medical professionals to be able to give a diagnosis almost immediately after

receiving a patient's MRI scan. This would revolutionize the way AD is diagnosed and would help millions around the world take early action on this disease.

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Artificial Intelligence and Positive Psychology in Practice By Zihan Liu

In recent days, artificial intelligence(AI) has come into our view, especially since the emergence of OpenAI Chatgpt. Apart from influencing fields of arts, such as painting and music-making, Artificial intelligence(AI) has also drawn the attention of psychology practitioners. Modern technology has been developing increasingly ever since three decades ago. Artificial intelligence is now a prevalent technology affecting almost every aspect of a human's life. AI is a computer system, which resembles human intelligence and performs tasks that used to require human efforts. The example includes reasoning, visual and auditory perception and decision-making. Until recently, artificial intelligence has become able to work without human input by applying learning algorithms to identify patterns, transforming human life into a new era (Renaud, 2023.6)

Since 1998, Positive Psychology has been brought out as the study of happiness, well-being, human flourishing as well as the other positive mental state of humans, as opposed to traditional psychology investigating mental illness. Positive Psychology Intervention (PPI) good, a newly formed approach using in Psychotherapy, is based on Positive Psychology, which joins together symptoms and strengths, risks and resources, weaknesses and values, as well as regret and hope get an exact definition of positive psychology(Duckworth, Steen &Seligman, 2005) PPI mainly helps patients practice to balance their strengths and weakness, using their best available resources to tackle with challenges in life , living a flourish, satisfied and meaningful life. (Rashid & Seligman, 2020)

Misery, conflict, reduction of pain, mental illness are the main areas that psychologists have focused on over the last centuries. While traditional psychology generally adopted a deterministic view, believing that a person's past determines his or her future, and focused on re,owing problematic stimuli , a new approach of psychology, Positive Psychology developed by Martin Seligman over 20 years ago, served to focus on people's strengths and make them flourish. (Seligman, 2003). When Dr. Seligman became the President of American Psychological Association (APA), his priority as president and a positive psychologist was to combine practice and science, and conduct studies on well-being. The aim of positive psychology is to bring people from the neutral state of mental health, which is supposed to have gotten rid of the negative feelings state, to the more positive, thriving state (Peng, 2020.8). This means moving people's mental well-being on a scale from -1 to 0 is not enough, and what positive psychologists will do is bring the score from 0 to +1. The main research area of Positive Psychology includes Character strengths, learned optimism, hope circuit etc. Seligman and his fellow researchers have operationalized the concept of PP to the model PERMA, which stands for Positive emotion, Engagement, Relationship, Meaning and Accomplishment (Seligman, 2011). Until now, the studies, outcomes and training in this field have been applied from school education to soldiers in the army, which makes it a historical revolution in psychology, and a turning point in human destiny (Peng, 2020.8).

While AI offers the vast potential to revolutionize nearly every aspect of human life, one

of the fields that AI will bring potential benefits is Psychotherapy(Renaud, 2023.6) Therefore, it is important for positive psychology practitioners to have a full knowledge of the implications of AI in clinics, and it is for them practitioners to decide how they are going to lead the development of AI in Positive Psychology (PP) and Clinics(Renaud, 2023.6). Positive psychology is a combination of symptoms and strengths, risks and resources, weaknesses and values, as well as regret and hope (Duckworth, Steen &Seligman, 2005)

Psychotherapy, one of the many applications of AI, has the potential benefits to enable AI to lower psychological practitioners' workload. For example, AI help clinicians with intake interviews, documentation, notes and other basic tasks (Walsh, 2023.6), also help with careful differential diagnosis, treatment conceptualization and big-pictures insights, the low-level tasks for diagnosis and treatment like symptom-tracking questionnaires or progress note could be handled by AI (Strade, 2023). These free up clinicians to do their best.

As AI developed, chatbots that help with therapy have been invented increasingly. One example is OpenAI ChatGPT. ChatGPT is able to carry out almost human-like conversations. It has the capacity to predict human's next possible words in conversation (Reardon, 2023.6). Users have provided positive feedback, like "ChatGPT is better than my therapist", "I feel heard by ChatGPT", given that ChatGPT can listen to a person's thoughts, and respond to him or her while the person talked about their encountered struggles (Reardon, 2023.6).Other mental health service AI chatbots include Woebot, Tess and Google bard. There are AI chatbots for other purpose, such as Large Language Model (LLM), which used in clinics due to its capacity to switch different personas (Reardon, 2023.6). LLM can ask a user questions and draw accurate conclusion from users' given information (Reardon, 2023.6). Another one, Limbic, is used to diagnose certain mental health illness at the U.K.'s National health Service (Reardon, 2023.6) .

Although it is admitted that the potential values of AI have been demonstrated, there are other risks and issues to be concerned. For example, chatbots may show biases and discrimination about socioeconomic status and racialism, or they may leak out user's privacy and destroy the data security, or what's more, replacing human interaction and empathy etc(Renaud, 2023.6). Overall, the principles and laws of AI usage are under review. Mental health and clinical professionals are going to develop proper guidance that integrate AI and traditional clinical sessions further and better. Positive Psychology practitioners are going to work with data scientists and technology engineers to ensure AI is used for greater good of human beings instead of causing disruption (Renaud, 2023.6).This paper is going to explore how positive psychologists can help AI used responsibly and ethically to maximize its potential for enhancing well-being, and how AI and positive psychology play the essential role in shaping our future. The Search database is Google Scholar. The Search query used was ("Artificial Intelligence" AND "Positive Psychology Interventions"). There were no limitations of time set for the articles published. Using Positive Psychology, AI will be able to positively impact the mental health landscape.

Increasing demand for mental health service

Research suggested that there are approximately 1 out of every 5 adults in United States (U.S.) suffer from mental illness (*Lifetime Prevalence of Mental Disorders in U.S. Adolescents: Results from the National Comorbidity Survey Replication–Adolescent Supplement (NCS-A) - Journal of the American Academy of Child & Adolescent Psychiatry*, n.d.) (*Key Substance Use and Mental Health Indicators in the United States: Results from the 2019 National Survey on Drug Use and Health*, n.d.), (*NIMH » Mental Illness*, n.d.). while in one nationally representative sample, only 41.1% of U.S. adults with a diagnosis of anxiety, mood, impulse control and substance disorders received treatment in the previous 12 months (Wang et al., 2005).

As mentioned in the introduction, the 21st century becomes a new era, which enables PPIs and technology to be integrated (Villani et al., 2016). The utilization of technology becomes increasingly important given the demands for mental health services, especially when there are barriers preventing people from receiving help, including shortage of mental health professionals, perceived stigma, socioeconomic status etc. need citation AI and positive psychology, however, can be combined together, to resolve these issues. AI has the potential to deliver interventions with the help of the Internet and apps, therefore increasing the access Positive Psychology, which works on joy, gratitude and character strengths, can buffer the negative emotions like anxiety and distress, and also prevent the occurrence of depressed emotions beforehand. This paper is going to explain the specific way of achieving these effects. This ain't the intro any more stop saying that this paper will show. Write a conclusion sentence

PP2.0 and the New era of technology for humankind

Over the last 30 years, the pioneers of Positive Psychology (PP), known as PP1.0 has been developed and brought a new dimension to mainstream psychology (Mayer & Vanderheiden, 2020a). PP2.0, a more recent positive psychology, serves to improve previous drawbacks and provide PP a new direction (Wong, 2019), (Yakushko, 2019). This approach focus on both negative and positive situations, and by a subtle appreciation of the ambivalent nature of the good life (*The Deep Psychology of Eudaimonia and Virtue: Belonging, Loyalty and the Anterior Cingulate Cortex | Request PDF*, n.d.), (Mayer & May, 2019).

In this technology-driving new era of human being, changes occurring in different aspects of life require new research, new methodologies and new adjustments of positive psychology combined with those advancements of smart technology, artificial intelligence, algorithms and robotics, thereby leading to changes in meaning in life or work (Mayer & Vanderheiden, 2020b)

By integrating the technology and PP2.0, humankind is going to enter this new era, a turning point of human history that may change human destiny, although it is still under question whether this change is overall beneficial or is going to be alarming. Using the PP 2.0 framework, individuals will be able to see increased benefits versus PP 1.0 to mental health services.

Digital mental health interventions and AI

When it comes to AI systems in mental health service, there is a kind of AI-driving

software, known as AI chatbot, and also known as conversational agents or relational agents(Boucher et al., 2021).. As for mental health applications, there are about more than 10,000 of them currently available for download (Torous & Roberts, 2017). At the same time, lately, mental health industry is incorporating AI into existing platforms to carry out AI-guided products, which include health communication, virtual reality, symptoms and biomarker monitoring(Onnela & Rauch, 2016), (Abashev et al., 2016), (Baker et al., 2020). Digital Mental Health Interventions(DMHIs) are, therefore, being open to a large population, including children, teenagers, adults and elderly people. These people could be provided DMHIs if needed by having conversation with AI chatbots on the Internet(*(PDF) Usability Assessment of Interaction Management Support in LOUISE, an ECA-Based User Interface for Elders with Cognitive Impairment*, n.d.) and specific clinical population (Greer et al., 2019).

Currently, chatbots are not only being used as health assistants personally to improve people's well-being and helping with their mental health check-ins during and after their clinical session (Davis et al., 2020), but also facilitate the effects of therapy by providing access enabling people to transfer their therapeutic content into everyday life, check their progresses, and deliver other useful mental health result to give personal support. (*The Next Generation: Chatbots in Clinical Psychology and Psychotherapy to Foster Mental Health – A Scoping Review | Request PDF*, n.d.).

Some research found that participants will respond to AI generating situations with a subjective, behavioral and physiological level the same as when the situation is real, given that they know it is virtual characters and environment that they are communicating with (Villani et al., 2016). Other research suggested that people prefer to release their painful thoughts to media-mediated electronic doctors, rather than human doctors (*Yoshida, A., Hagita, Y., Yamazaki, K., & Yamaguchi, T. (1993). Which Do You Feel Comfortable, Interview by a Real Doctor or by a Virtual Doctor? A Comparative Study. Proceedings of the 2nd IEEE International Workshop on Robot and Human Communication (Pp. 370-374) - Google search*, n.d.) One example of a mental health system is "Ellie", who was developed at Institute for Creative Technologies as a virtual psychologist, being able to analyze people's words and their manners thus deciding their emotional state(Villani et al., 2016). Other kinds of AI systems were designed voice-based to support psychological professionals during diagnosis(Villani et al., 2016).

While still in the beginning stages, AI chatbots, like "Ellie", are proving beneficial in the provision of improved mental health services. With these chatbots, the mental health service industry will be able to deliver help to a wider range of population.

AI Chatbots— Anna, Vivbot and Youper

Generally, chatbots are perceived to be less judgemental, more objective in comparison to human doctors, which makes some people prefer to interact with chatbots more than human mental health practitioners (*Response to a Relational Agent by Hospital Patients with Depressive Symptoms | Request PDF*, n.d.) (Greer et al., 2019) (Lovejoy et al., 2019), (Radziwill & Benton, 2017). This makes users' self-disclosure easier, encouraging more conversational

flexibility(Greer et al., 2019), (Lovejoy et al., 2019), (Radziwill & Benton, 2017). Therefore, this trend indicates that those who would otherwise not find professional help will be able to receive healthcare through AI chatbots(Boucher et al., 2021).

When it comes to benefits, participants will experience increased accountability when using chatbots in their mental health service, and therefore having higher and more regular engagement (T. W. Bickmore et al., 2010), (Perski et al., 2019). Also, they will perform more intentions and behaviors to use the program(*(PDF) A Chatbot System for Mental Healthcare Based on SAT Counseling Method*, n.d.). In addition, users can engage with the therapy and the material more deeply(Donkin et al., 2011). Evidence can be found in another study, where participants using a mobile intervention perceived the guidance and direction offered by the chatbot in the program as beneficial (Ly et al., 2017). However, there are no studies that have explored the long-term impact of chatbots on engagement or dropout rates (Boucher et al., 2021).

On the contrary, there is variability in how people perceive chatbots. In one study, 32% of participants rated the chatbot was unhelpful (Inkster et al., 2018). In some cases, users have even reported that their interactions with the chatbot bothered them (Inkster et al., 2018), or that the chatbot was self-focused (Inkster et al., 2018) or annoying (Greer et al., 2019).

Only a few studies have tested the actual improvements in outcomes of using AI chatbots (Boucher et al., 2021). Most of these studies did not include a control group as baseline comparison. Therefore the results may be invalid (Boucher et al., 2021). This matters, especially when some researchers have been arguing that the therapeutic outcome may be due to placebo effect more than its own availability (Torous & Firth, 2016). What's more, most evidence are found for effectiveness in reducing depressive and anxiety symptoms, relatively small amount of studies have shown improvements in psychological well-being after two weeks compared to control group (Ly et al., 2017)

While individual feedback from patients about chatbots has been mixed, the research indicates that overall they have a positive impact on mental health treatment using positive psychological principles. There are several chatbots which have already overcome some barriers and showed positive influence.

Across several studies, a significant number of users complained that the conversation with chatbots could be repetitive(Ly et al., 2017), (Fitzpatrick et al., 2017), (T. Bickmore et al., 2005), which makes the chatbot feel less humanlike (Ly et al., 2017) and reduces users' motivation to continue the program (*(PDF) Chatbots: History, Technology, and Applications*, n.d.). In the absence of mental health professionals, users, especially those who lack confidence in their ability to improve their mental health, are more likely to end their session, thereby leading to high drop-out rate. (Boucher et al., 2021).

Anna, the Happify Health's AI serves to overcome this concern. Anna is another AI-based chatbot, which models a therapist to help users complete Happify activities (Boucher et al., 2021). It is carried out by Happify health in 2019, to incorporate into its commercial digital mental health platform(Boucher et al., 2021). For example, Anna will deliver evidence-based games, which integrate with various therapeutic approaches, including CBT, mindfulness-based

stress reduction, and more importantly, Positive Psychology Intervention(Boucher et al., 2021).

Anna has human-like social features like empathy and meta-relational communication, which improves the bonds between human users and artificial therapists (Boucher et al., 2021). Participants can follow the recommended practices with Anna.(T. Bickmore et al., 2005), (*(PDF) Best Practices for Designing Chatbots in Mental Healthcare – A Case Study on iHelper*, n.d.). For instance, to reinforce rapport, Anna calls users by name in conversation, and shows curiosity in their communication by leading them to offer background information and relationships with others, when such information is mentioned in the normal course of conversation (Boucher et al., 2021). Besides, it further communicates people's interest and shows understanding by asking clarifying questions and content-mirroring responses, and follows up input in their conversation with users (Boucher et al., 2021)

Anna usually begins by greeting users with an introduction and explanation of the chatbot's role within the track, which may include surface-level information (e.g. noting how often the user logs on) or reference more personal information acquired in previous conversations, and then ask users specific questions to gather information that can be used to better personalize the routine (Boucher et al., 2021). By delivering activities within these tracks, participants will have deeper engagement and adherence (Boucher et al., 2021). Apart from that, for each activity, Anna can track the criteria that are important to reach optimal outcomes, such as reviewing the responses based on these criteria, then leading users to give expected information which is initially lacking, thus maximizing the benefit associated with the activity (Boucher et al., 2021).

Still, research for Anna is in preliminary stages (Boucher et al., 2021). In some pilot studies, users reported mostly positive perceptions of Anna, such as rating Anna as helpful and showing high engagement in the interventions(Boucher et al., 2021). Also, Anna makes people, who have lower levels of mental health self-efficacy, feel more confident in their ability of mental health management, when the intervention is completed. (Boucher et al., 2021).

In Facebook Messenger, there is a chatbot called Vivbot, which is invented by Hopelab in San Francisco, serving to delivering pre-written materials and Cognitive Behavioral Intervention to users, based on Stress and Coping strategies, Broaden-and-Build theory, as well as skills of Positive Psychology (Greer et al., 2019).

There is a pilot randomized controlled trial testing the engagement, feasibility, usability and initial efficacy of Vivbot, and the effects of Positive Psychology skills delivered through Vivi Bot chatbot on reduction in depression, anxiety, negative emotions and increase in positive emotions, done on participants who were suffering from cancer, aged 18-29 years (Greer et al., 2019). Apart from obvious reduction of anxiety and negative emotions in experimental group more than control group, results also show that experimental group showed higher engagement, and interest in positive psychology content, though control group showed greater increase in positive emotions, perhaps through the daily rating of emotions they were set to complete (Greer et al., 2019). Particularly, participants found positive psychology skills helpful, since their positive emotions were stimulated, with mediating factors like changing healthy behaviors,

improved psychosocial functioning, increasing positive resources, altogether resulting in health outcomes (Greer et al., 2019). Overall, the results made bot-based intervention and positive psychology skills promising in the future (Greer et al., 2019).

It should be noted that, also, for this study, although their results are inspiring and promising, there are limitations. For example, including only cancer patients and young participants, therefore a small population size, the generalizability of the study is low (Greer et al., 2019).

Youper is an empathetic, safe and clinically validated chatbot for mental healthcare(*Youper*, n.d.). Having supported the mental health of over two million people, the groundwork of Youper is evidence-based interventions-treatments that have been studied extensively and proven successful, and proven clinically effective at reducing symptoms of anxiety and depression by researchers at Stanford University (*Youper*, n.d.).

In a study, which has 5943 participants to download Youper between March 4, 2020 and July 10, 2020, has provided evidence of Youper's acceptability in everyday life's setting (Mehta et al., 2021). These studies highlight the positive impact of Youper, proving it as low-cost, light-touch intervention that improves mental health for people around the world, and having the highest retention rate for users compared to other AI chatbots (Mehta et al., 2021). Results indicate that the effectiveness of the emotion regulation practice is able to predicts the long-term impacts of app use on symptoms reduction (Mehta et al., 2021).Although the population size of the Youper study, having thousands of users as participants, it lacks the control group to ensure the effects were truly generated by the app (Mehta et al., 2021).

These AI chatbots proved that AI is able to carry out human-like conversation, showing empathy and making users engage and feel understood. Through chatbots, AI can help with users' daily emotional regulation, management of stress and anxiety, and more importantly, help users with positive psychology practice and increase their level of well-being. Although they are still in the preliminary stage, their potentials are significant.

Artificial Intelligence in Positive Organizational Psychology

Positive Organizational Psychology (POP), defined as "The scientific approach of one's positive subjective experiences and traits in the workplace and organizations, and its application to improve the quality of experience in those workplace and organizations (*(PDF) Positive Organizational Psychology, Behavior, and Scholarship: A Review of the Emerging Literature and Evidence Base*, n.d.), and draws from the developments in positive organizational behavior (Luthans & Church, 2002) and positive organizational scholarship (*Cameron: Positive Organizational Scholarship: Foundations... - Google scholar*, n.d.).

POP 2.0 is the study extended from of POP, whose important line of work is known as positive approaches to diversity, equity and inclusion (Rao & Donaldson, 2015), (*Reinvigorating Research on Gender in the Workplace Using a Positive Work and Organizations Perspective* - Warren - 2019 - International Journal of Management Reviews - Wiley Online Library*, n.d.), (*Donaldson: Evaluating Positive Psychology Interventions... - Google scholar*, n.d.). In general,

POP 2.0 adopts human-centered technological innovations (*Full Article: Positive Organizational Psychology 2.0: Embracing the Technological Revolution*, n.d.). In fact, it embraces and facilitates optimal functioning in organizations, by creating innovative interventions, enhancing collaboration between stakeholders, and improving wellbeing in both physical and virtual/digital environments (*Full Article: Positive Organizational Psychology 2.0: Embracing the Technological Revolution*, n.d.). POP2 introduces new technological solutions to examine, predict and form the positive states, traits and behaviors associated with optimal organizational functioning (*Full Article: Positive Organizational Psychology 2.0: Embracing the Technological Revolution*, n.d.)

While artificial intelligence is commonly perceived as an innovation that will significantly change people's performance in daily workplace activities (*The Impact of Artificial Intelligence on Industrial-Organizational Psychology: A Systematic Review | The Journal of Behavioral Science*, n.d.), it also has particular implications for organizational and industrial workers (*Human Trust in Artificial Intelligence: Review of Empirical Research | Academy of Management Annals*, n.d.). The "fourth industrial revolution", driven by artificial intelligence, carrying out the transfer of human's agency and autonomy to computer-driven technology (*Human Trust in Artificial Intelligence: Review of Empirical Research | Academy of Management Annals*, n.d.).

In the coming years, there is a new wave of research accumulating in POP 2.0, based on topics like social and organizational network analysis of artificial intelligence-driven positive organizational interventions, human-robot collaboration (Donaldson et al., 2022). This new trend will result in rapid innovation, massive adoption of artificial intelligence systems, machine learning, social media analysis, big data analysis, which we will learn immensely from during POP 2.0 (Donaldson et al., 2022). These rapid changes need the help of sophisticated models, approaches and measures, being flexible to adapt to the new innovations and discourses in technology and the discipline (Donaldson et al., 2022). PERMA +4, introduced as the first model in the new innovations, has its effectiveness proven effective and can combine with AI systems to drive the innovation further in the well-being and sustainable work performance space for POP 2.0.

Apart from the rapid rise and utilization of artificial intelligence (AI) in Psychology in mental health service intervention, a rise in AI-driven positive psychological interventions, specifically within organizations, ranging from AI-Coaching to AI-driven chatbots aimed at enhancing wellbeing is expected to see (Greer et al., 2019). These chatbots do not require active input from a therapist, coach or practitioner, but instead perform its perceived accessibility and usefulness themselves(Donaldson et al., 2022). Therefore, AI allows for intervention content to be generated and used when it is needed and eliminates the delay time between the experience of a problem and a potential solution (Greer et al., 2019). The use of chatbots is still rare within organizational contexts, but will become increasingly important over the next two decades (Laranjo et al., 2018).

Technologists should integrate the principle of using human-centered technology, such as

AI, to ensure that they enhance rather than replace human experiences and relationships (*Full Article: Positive Organizational Psychology 2.0: Embracing the Technological Revolution*, n.d.). Like it is in the case of mental health service, there are several challenges or ethical implications of AI in organizational and industrial approach. One concern is that it may impair workers' engagement. Using artificial intelligence and machine learning in the real-time active assessments of positive state can be passive for aspects such as work engagement, such as monitoring email and workflows (*Full Article: Positive Organizational Psychology 2.0: Embracing the Technological Revolution*, n.d.), which thereby impairing their perceived happiness during the work. The proliferation of AI technologies has introduced a new type of psychological contract, named "alienation", which has special implications of POP and Industrial Organizational Psychology (IOP) practitioners (*The Impact of Artificial Intelligence on Industrial-Organizational Psychology: A Systematic Review | The Journal of Behavioral Science*, n.d.). The study by (Koo et al., 2021) demonstrated that perceived job insecurity resulting from the implementation of AI-enabled technologies significantly affected perceived job insecurity, perceived job engagement. Furthermore, AI raises concerns about privacy and confidentiality just like it is for chatbots to provide counseling for people, and creates the potential for biased decision-making in the workplace (*Full Article: Positive Organizational Psychology 2.0: Embracing the Technological Revolution*, n.d.). Further bias, perpetuating existing inequalities and facilitating further discrimination (*Full Article: Positive Organizational Psychology 2.0: Embracing the Technological Revolution*, n.d.). Overall, POP researchers and practitioners required ongoing learning to keep abreast of the latest tools, techniques and platforms.

While there are some concerns, overall research suggests that by using principles of positive organizational psychology and AI, there is improvement in the working environment and productivity as well as mental health in the workplace.

Artificial Intelligence on College students' well-being

College students' mental health issues are rising alarmingly (Benton et al., 2003). In 2018, about 85% of college students in the USA reported feeling "overwhelmed by all they had to do" and nearly 43% reported "feeling so depressed that it was difficult to function" at least once within the last 12 months (*NCHA-II_Fall_2018_Undergraduate_Reference_Group_Executive_Summary.Pdf*, n.d.). Depression and anxiety are reported as the top hurdles to academic achievement (Breslau et al., 2008) and have a long-lasting effect on students' occupational (*The Impact of Psychiatric Disorders on Labor Market Outcomes - Susan L. Ettner, Richard G. Frank, Ronald C. Kessler, 1997*, n.d.) and social (Kessler et al., 1998) outcome also.

In the past, many studies have reported positive association between college students' psychological well-being, mood and readiness to change for better well-being and robotic intervention (Jeong et al., 2020). These kinds of mental health problems are under demand, since universities are not currently designed to cater all the personal and emotional needs of students (Dekker et al., 2020). In a study, life-crafting intervention has been introduced.

Life crafting intervention has a process in which people actively reflect on their present and future life, set goals for important areas of life, such as social, career, and leisure time, and, if required, participants can make concrete plans and undertake actions to change these areas in a way that is more congruent with their values and wishes (Schippers & Ziegler, 2019). This can be online and scalable.

As students struggle with academic achievements and mental health problems during their adoption from high school to tertiary education, healthcare professionals sought to find out the possible solutions that integrate contemporary AI solutions and effective positive intervention, and the later one could be the life-crafting intervention(Dekker et al., 2020). One advantage is the scalability of life-crafting intervention. With a low threshold, the intervention may contribute to early detection of mental health issues, thus solving the problems of students in an interactive and personalized way(Dekker et al., 2020). This focus tackles the problems that when one seeks help for their mental health problems, he or she is likely to bear perceived stigmas from the surroundings(Dekker et al., 2020). With AI chatbots and the life-crafting intervention, students can instead ask for help anonymously, without rising the perceived stigma problems from people around them, which also leads to more of their self-disclosure and rapport (Lucas et al., 2014), (*Frontiers | Reporting Mental Health Symptoms: Breaking Down Barriers to Care with Virtual Human Interviewers*, n.d.). On top of that, having a positive focus on life crafting and setting personal goals throughout this process decreases the correlation with stigma of mental health problems(Dekker et al., 2020).

Specifically, this intervention mainly helps in two ways. Firstly, life-crafting intervention integrated into the chatbot will make students more aware of their goals and potential obstacles during their process to reach their goals (Dekker et al., 2020). This will help them to set priorities for themselves, and may also encourage them to seek help for their problems in an early stage (Dekker et al., 2020).

Secondly, the chatbots are able to recognize the signals to academic or mental health problems, immediately offering in-app coaching if they detect mild problems, or referring users to professional help for more severe problems in an early stage(Dekker et al., 2020). Furthermore, An additional advantage is that mental health chatbots often have higher adherence rates than other internet-based mental health care (Dekker et al., 2020).

In the future, research should focus experimentally on the effects of interventions that combine insights from positive psychology which lend itself for curriculum wide implementation with the interactive potential of a chatbot (Dekker et al., 2020). Ideally, AI chatbot intervention will be able to optimize both student well-being and academic achievement (Dekker et al., 2020).

In the upcoming study, research should also focus experimentally on the effects of interventions that combine insights from positive psychology which lend itself for curriculum wide implementation with the interactive potential of a chatbot (Dekker et al., 2020). Ideally, AI chatbot intervention will be able to optimize both student well-being and academic achievement (Dekker et al., 2020).

Using AI and positive psychology principles, research suggests that mental health and through that academic performance can be improved in the college population and that interventions, such as life crafting, can be delivered more widely.

Concern and criticism of AI

The main concerns including lack of guidance, perceived stigma----People may consider involving in mental health care seems problematic, security and privacy-----Worries about personal information may leak out or being used in the program, and biases and discriminations showed by AI, especially when AI being used in criminal sentencing shows racial bias which lead to unfair outcomes (Renaud, 2023), although another evidence shows users would be less morally outraged by gender discrimination caused by an algorithm as opposed to discrimination created by human (*AI Is Changing Every Aspect of Psychology. Here's What to Watch for*, n.d.). Trust is needed to be established when working with AI, since the highly personal and sensitive nature of mental health information highlights the need to ensure that sensitive patient data is adequately secured and protected (Boucher et al., 2021). Therefore, discussion of ethics, privacy, confidentiality and safety are required (*(PDF) CONTEXTUAL DIFFERENCES IN THE DYNAMIC MEASUREMENT OF TRUST IN WEBSITES*, n.d.).

It is worth noting that, although AI chatbots are useful and innovative, there are several things to improve. Firstly, currently these chatbots are mainly designed for depression or anxiety, (*(PDF) A Review of Mobile Chatbot Apps for Anxiety and Depression And Their Self-Care Features*, n.d.). Secondly, it is criticized for high dropout rates and low engagement (Boucher et al., 2021). Furthermore, AI chatbots didn't make difference in engagement, adherence, and sometimes outcome improvement than human-driving therapy, although therapists or peers or other non-clinical support agents are involved (Boucher et al., 2021). Accuracy, trustworthiness and privacy of chatbots all emerge as the potential barriers to engagement and adoption of methods being introduced (Kretzschmar et al., 2019). Other potential factors could be related to chatbot's personality, emotional responsiveness, and empathy (Yu et al., n.d.) (T. Bickmore et al., 2005). In the future, appropriate guidance and feedback should be considered provided, and developed more to enhance positive psychological constructs, such as psychological well-being, mindfulness, self-efficacy, self-esteem and resilience.

Other criticism includes lack of empathy shown by AI. It is obvious that users prefer chatbots that are designed to display empathic reactions more. It is a beneficial sign that in some global surveys, participants show a general positive attitude in terms of empathetic care. Some people found chatbots buffer the negative effects from ostracism (de Gennaro et al., 2019). At the same time, certain AIs show significant strengths. For examples, ChatGPT is better than previous AIs at interpreting the meaning of human's question and responding in a realistic manner, and Large Language Model (LLM) could even offer better responses than therapist (*AI Chatbots Could Help Provide Therapy, but Caution Is Needed - Scientific American*, n.d.). However, replacing human interaction, empathy and touch can be a concern. Positive Psychologists should ensure

that a human coach is still vital to the success of the relationship, while AI is a helpful tool but not used as replacement (*Full Article: AI Assistance for Coaches and Therapists*, n.d.).

Apart from carrying out more precise measures, researchers should focus on their delivering of positive psychology interventions in upcoming research. Although these two apps allow access across demographic and other barriers to serve the demand of mental health, it is mainly used by the clinical population who suffer from depression and anxiety, for instance. The reduction in negative emotions does not guarantee the increase in well-being outcomes. To make it used more widely and serve a larger population's needs, Positive Psychologists should work with designers of these apps to consider adding positive psychology principles, or activities, like mindfulness meditation and gratitude exercise, which can also buffer the negative impact resulting from stress, depression and anxiety.

Finally, there still are not enough studies to prove the effectiveness with AI in mental health care currently(Boucher et al., 2021). In the future, aside from testing users perceptions of AI, developers of mental health chatbots need to consider this as a task that requires collaboration between themselves, mental health professionals and users/patients in order to develop chatbots that meet users' needs, goals and lifestyles, ensuring trust in AI, and more importantly, improving mental health outcome (Boucher et al., 2021)

Although there are concerns over lack of regulation with regard to AI, research demonstrates definite benefits to using these technologies and so legislators may wish to create guidelines to allow this technology to help as many people as ethically and efficiently as possible.

Discussion

In the 21st century, not only have mental health circumstances become severe while there is lack of mental health intervention service, but also humankind has come to an age of technology and positive psychology. Therefore, Artificial Intelligence chatbots delivering positive psychology intervention offer an ideal way to serve the need of mental health service, as well as engaging people to positive psychology.

There are many AI chatbots in the market that have received positive feedback from users, including Happify Health's Anna, Vivbot, Youper, Woebot, Wysa, Tess etc. Apart from applying in healthcare service, there are AIs applying in many field, such as applying in the workplace by combining with Positive Organizational Psychology, in college through intervention such as life-crafting for students to relive study stress and better adapt to their transition to college academics, and for patients who received cancer treatment. Whether or not they are specifically aiming for Positive Psychology practices, they have helped handle anxiety and depression, and enhance the well-being of a large number of users. These AI's wordings are more human-like and sensitive than before, which make users think AI can indeed understand their feelings, reaching the same effects of working with therapists face to face. In the future, the ability of AI to understand human's language and provide accurate responses may be improved further.

Basically, one existing drawback is that most currently popular AIs are designed for patients who require clinical therapy, which means they aim for negative syndrome. In the future, psychologists could work with technological designers to create AI that applies positive psychology, to serve the needs of a larger population of people by improving their happiness level, engaging them in positive psychology practice. After all, reducing negative syndromes does not mean increasing positive syndromes.

Another drawback is although these AI chatbots have served a large number of users, they are still not prevalent enough. There are still many people who need psychological help but have no idea of AI chatbots and their usefulness. Apart from that, these AI chatbots mentioned above are only accessible in local countries. Other countries in the world can't approach them. Therefore AI chatbots are still under development, and in the future it may be more common all over the world.

Overall, in the future, positive psychologists may work with data scientists and engineers to design algorithms and machine learning models informed by expertise in human behavior and emotions, helping create ethical standards, helping research and training, thereby guiding the development (Renaud, 2023). They should be focusing on training of health professionals, filling the gaps in ethical and regulatory frameworks, misuses of AI, or any other specific ethical and social issues during mental health intervention with AI (Fiske et al., 2019).

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Modeling the Water Temperature Profile of Lakes: A Physics Informed Neural Network (PINN) Approach By Audrey Creighton

Abstract

Water temperature plays an important role in our environment and is applicable to nearly all limnology research, as the temperature of a body of water affects biological activity and growth of organisms such as algae and bacteria. Certain organisms have a preferred temperature range within which they can survive, while others become dormant or die when the water reaches extreme temperatures. The temperature of water also governs the maximum dissolved oxygen concentration of water. Dissolved oxygen in water is important for aquatic life because of its vital role in cellular respiration. Predicting water temperature is also an important factor in determining whether a body of water is acceptable for human use. Warm bodies of water may contain pathogens that can be dangerous to humans.

Our research presents a computational method of determining lake water temperature through a novel technique known as physics-informed neural networks (PINNs). PINNs can be used to model and forecast the temperature of water over a specific time period by training a neural network using the data points derived from the discrete form of a partial differential equation and taking into account the boundary conditions. Several factors such as wind, precipitation, and solar energy effects on water temperature were investigated. By using a computer simulation in place of an analytical mathematical model, a tremendous increase in run time speed can be achieved. The results can be used to determine the patterns in water temperature throughout a year, demonstrating the advantages of a PINN over an analytical model.

Introduction

Computer simulations are important tools in many areas of research. Generally, computer simulations are accomplished using traditional numerical methods, such as the finite difference method, finite element method, or computational fluid dynamics. While these methods are accurate, they can be slow and time-consuming. Traditional methods use a process called "time stepping" that requires the solution to be computed one time step at a time in chronological order. For example, if we wanted to compute the solution at time 1000 seconds, we must know the solution at time 0.1 seconds, time 0.2 seconds, time 0.3 seconds, all the way up to time 1000 seconds. Recently, scientists have found that one way to make computer models faster is to solve them using neural networks instead of traditional numerical methods. What makes neural networks so much faster is that they can jump ahead to any time step within their training domain. This means that, with a neural network, we can compute the solution at time 1000 seconds as quickly as you can compute the solution at time 0.1 second.

In this research, our goal is to use a neural network to solve for the temperature profile of a lake. The neural network can compute the temperature profile at any time of the year. Additionally, the neural network can compute the solution magnitudes faster than a traditional

numerical solver. Our research aims to prove the ability of neural networks to produce practical and accurate computer models that are amongst the fastest in the world.

Methods

In order to train a neural network to predict the temperature profile of a lake, we conduct two major processes:

Method 1: Build a custom, discretized 3D mathematical model of transient heating using partial differential equations to model the temperature profile of the lake;

Method 2: Subsequently, apply the resulting data and use it to train a neural network. The end result will be a neural network that performs nearly the exact same computations as an analytical mathematical model but with a tremendous speed advantage.

A. Method 1 of 2: Build a mathematical model of the transient heating of a lake in order to collect collocation data.

Step 1: Represent the lake as discrete points using Microsoft Excel CSV

To determine the transient heating inside of a lake, we will convert our lake profile into a 2D grid with 51 rows and 151 columns. We will convert the continuous nature of the lake profile into discrete points. That way, we only compute the temperature at a finite number of points.

Fig. 1 Outline and initial temperature profile of a "deep" lake
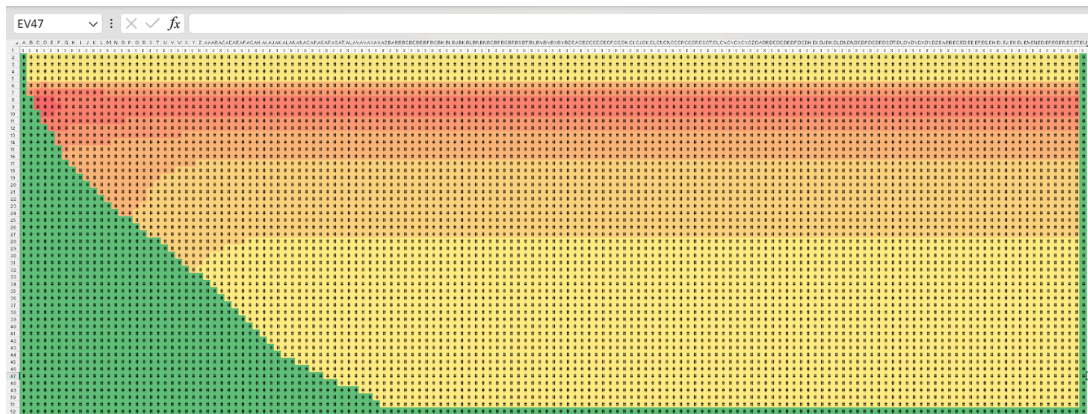
The image, which was created in a Microsoft Excel CSV file, consists of 51 rows (excluding the header) and 151 columns. Thus, we have broken our environment into 51*151 = 7701 discrete points. However, the 1183 green-colored cells represent the area

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that lies outside of the lake, i.e., rocks and soil. This means that our lake is broken into 7701-1183 = 6518 discrete points. The green cells to the left and bottom of the image represent earth material while the green cells to the right of the image represent an axis of symmetry. Establishing an axis of symmetry is a mathematical trick that allows us to simulate only half the lake, thereby reducing the needed number of computations.

Fig. 2 . Outline and initial temperature profile of a "shallow lake."
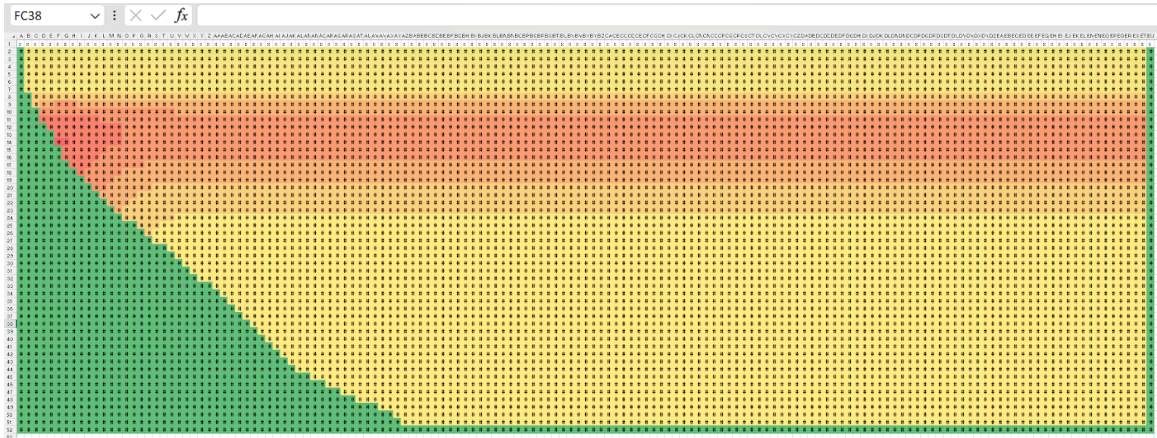
Again, the image consists of 51 rows (excluding the header) and 151 columns. The outline of the "shallow lake" is exactly the same as that for the "deep lake." The only difference is in the initial temperature profile of the lake. Because the lake is shallow (meaning that the differential spacing in the y-direction is smaller), the red band of warmer water is more spread out in the shallow lake profile than in the deep lake profile.

Step 2: Derive a formula to compute the temperature at every discrete point in the *interior* of our lake.

There is a partial differential equation known as the transient heat equation that represents the transient heating of a continuous material. (Pina, H.L.G., Fernandes, J.L.M. 1984) That formula is given here:

$$\frac{\partial^2 T}{\partial x^2} + \frac{\partial^2 T}{\partial y^2} + \frac{\partial^2 T}{\partial z^2} + \frac{\dot{q}}{k} = \frac{\rho C_p}{k} + \frac{\partial T}{\partial t}$$

This equation illustrates how the temperature of any point in 3D space varies according to the spatial coordinates x, y, and z, and the temporal coordinate t. However, our lake profile is 2D (which is equivalent to prismatic 3D), so we can drop the z-axis. This equation also includes a heat source q, which the *interior* of our lake does not have. Thus, for the *interior* points of our lake, we will use the following modified equation:

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$$\frac{\partial^2 T}{\partial x^2} + \frac{\partial^2 T}{\partial y^2} = \frac{\rho C_p}{k} + \frac{\partial \partial^2 T}{\partial t}$$

This equation is in a "continuous" form. Since we "discretized" our lake into discrete points on a 51 x 151 grid, we will need to replace the continuous form of the transient heat equation with a discrete form. This size grid was selected in order to properly display the lake proportions, while minimizing the number of points to make sure the neural network would not be overloaded. We accomplish this by replacing every spatial and time derivative with its finite difference form.

We insert the finite difference form of each term into the transient heat equation (Recktenwald, 2004), setting Δx=Δy, and rearranging, we obtain:

$$T_{i,j}^{k+1} = T_{i,j}^{k} + \Delta t \bullet \frac{k}{p \bullet c_p} \bullet \frac{1}{\left(\Delta X^2\right)} [T_{i-1,j}^{k} + T_{i+1,j}^{k} + T_{i,j-1}^{k} + T_{i,j+1}^{k} - 4T_{i,j}^{k}]$$

In this equation, the subscript "i" represents the index in the x-direction, the subscript "j" represents the index in the y-direction, and the superscript "k" represents the index in time. Thus, this equation allows us to find the new temperature $k+1$ at any point I,j using only the current temperature at time k. Specifically, we see that the temperature of any point in space is dependent on the temperature of the points in space around it. Given our point in space, the formula requires that we sum the current temperature at the point in space directly above, below, to the right, and to the left. Then, from this sum, we must subtract four times the current temperature at our point in space. This mathematical process simply represents the heat that a point can gain due to its temperature gradient with the four points around it. This new value is then multiplied by constant: $\frac{k}{p^*c_p} * \frac{1}{(x\Delta)^2}$ and Δt and added to the initial value of the temperature. This formula is simplified down from its original form to reflect a case where Δx is equal to Δy.

Step 3: Derive a formula to compute the temperature at every discrete point along the side and bottom edges of our lake.

In this step, we will derive a formula to compute the temperature along the left, right, and bottom edges. To accomplish this, we first have to understand what kind of boundary to apply to the left, right, and bottom edges. We will presume that, for the left and bottom edges of our lake, the heat inside the lake cannot escape. In other words, the left and bottom edges of our lake are well insulated. To prevent the heat from escaping, we apply a first-order zero-flux Neumann boundary to the left and bottom edges:

$$q_s = -k\frac{dT(0,t)}{dx} = 0$$

Because the right edge of the lake is an axis of symmetry, no heat should escape out of the right edge of our lake. So, we can also say that the right edge of our lake is well insulated. Thus, we apply a first-order zero-flux Neumann boundary to the right edge as well.

Step 4: Derive a formula to compute the temperature at every discrete point along the top edge of our lake.

Finding the formula for the discrete points along the top edge of the lake is the most difficult task, because we have a non-zero-flux Neumann boundary. This means that heat is allowed to enter and leave the lake's surface. In other words, heat transfer into and out of the lake is constantly occurring. The amount of heat transfer at any point in time is dependent on numerous weather conditions and other factors. The process to compute the temperature along the top of the lake is as follows.

q_total, the total heat flux into the lake in W/m2, is given by:

$$q_{solar} = q_{solar} + q_{sensible} + q_{latent}$$

q_solar is the solar radiation, q_sensible is the sensible heat flux, and q_latent is the latent heat flux.

q_solar, the solar radiation, combines the short wave radiation q_short and the long wave radiation q_long:

$$q_{solar} = q_{short} \bullet (1 - a) + q_{long}$$

α, the albedo:

$$a = p^{(c\sin\sin b+1)}$$

where

> a = hourly albedo,
> c = roughness coefficient,
> p = color coefficient,
> b = solar angle, in degrees.

H = solar hour angle, degree. (H = 0 at solar noon, 15° per hour deviation from solar noon, "+" in the afternoon, "-" in the morning)

The short-wave and long-wave radiation values are obtained from weather data The color coefficient p and the roughness coefficient c are found using the below table:

Fig 3. Values for the coefficients p and c (For 0.3 micron to 3-micron wavelengths)

```
Surface and                                                 Average
                                                               2
condition                              p         c          R
-----------------------------------------------------------------

Lakes and ponds, clear water
    waves, none                       0.13      0.29        0.817
    waves, ripples up to 1 inch       0.16      0.70        0.741
    waves, 1 inch or more with
           occasional whitecaps       0.23      1.25        0.827
    waves, frequent whitecaps         0.30      2.00        0.852

Lakes and ponds, green water,
    waves, ripples up to 1 inch       0.22      0.70        0.902

Lakes and ponds, muddy water
    waves, none                       0.19      0.29        0.758
```

The solar angle B and solar declination angle D are computed using these two formulas, where N is the Julian day:

$$B = \sin \sin D \; \sin \sin L \; + \; \cos \cos D \; \cos \cos L \; \cos \cos H \,)$$
$$D = 0.39797 \cos \cos [0.98563(N - 173)]\}$$

$q_{sensible}$, the sensible heat flux through the lake surface:

$$Q_s = - \, p_a \bullet c_p \bullet C_s\left(T_s - T_a\right)W$$

T_v, the virtual temperature:

$$T_v = T(\frac{1 + \frac{W}{E}}{1 + W})$$

ρ_a, the density of the moist air mass:

$$P_a = \frac{P}{(R_d \times T_v)}$$

ω, the mixing ratio:
$$W = \frac{Ee}{P - e}$$

e_a, the vapor pressure above the lake's surface:

$$e = e_0 exp\left[\left(\frac{L_v}{R_v}\right)\left(\frac{1}{t_0} - \frac{1}{T_d}\right)\right]$$

L_v, the latent heat of vaporization of water:

$$L_v = 2500297.8 - 2369T$$

$c_{p,a}$, the specific heat of moist air in J/kg-K:

$$C_p = C_{p0}\left(\frac{1+W\frac{C_{pv}}{C_{p0}}}{1+W}\right)$$

c_s, the sensible heat transfer coefficient:

$$C_p = \{W < 8\ ms^{-1}: (0.720 + \left[0.0175\ W\left(T_s - T_a\right)\right])\cdot10^{-3}\ W{\geq}8\ ms^{-1}: (1.000 + \left[0.0015\ W\left(T_s - T_a\right)\right]$$

q_latent, the latent heat flux through the lake surface:

$$Q_e = - P_a \bullet L_v \bullet C_e\left(q_s - q_a\right)W$$

q_s, the specific humidity at the lake surface:

$$q = \frac{Ee}{P-(1-E)e}$$

C_e, the evaporative heat transfer coefficient:

$$C_e = 1.5\cdot10^{-3}$$

Now that we know q_total (the total heat flux into the lake), the temperature of the nodes along the top edge of the lake can be computed using the finite volume method given below:

$$\dot{q}_s, T_\infty = 300, H_c$$
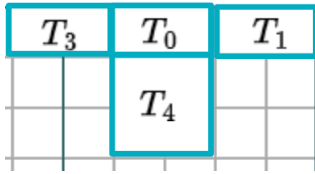
$$K \cdot \frac{T_1 - T_0}{\Delta x}\left(\frac{1}{2}\Delta y \cdot \delta\right) + K \cdot \frac{T_3 - T_0}{\Delta x}\left(\frac{1}{2}\Delta y \cdot \delta\right) + K \cdot \frac{T_4 - T_0}{\Delta y}\left(\frac{1}{2}\Delta x \cdot \delta\right) + q_s(\Delta x \cdot \delta) + h\left(T_\infty - T_0\right)(\Delta x \cdot \delta) = P\left(\frac{1}{2} \cdot \Delta x \cdot \Delta y\right.$$

To use this formula, we only need two last variables: T-infinity and h. T-infinity is just the common notation for the air temperature. So, we will obtain that at 15-minute intervals from our weather data. The last variable, h, is the convective heat transfer coefficient. This is given by:

$$h_c = 10.45 - v + 10^{\frac{1}{2}}$$

In this formula, "v" is just the wind speed (measured at 10 meters above the surface of the lake) in units of meters per second.

Step 5: Find the weather and material data necessary to run the model.

The formulas above require that we obtain certain data. For example, the transient heating equations require that we know the mass density ρ, specific heat capacity c_p, and thermal conductivity k of our lake water. These values, in turn, depend on the salinity of our lake. Assuming that our lake has a salinity of 15%, the aforementioned values will be $\rho = 1171.45$ kg/m^3, $c_p = 3681.75$ J/kg-K, and $k = 0.60$ W/m-K.

Additionally, to create a transient heat modeling for the temperature profile of our lake for a 12-month period, we will need a detailed set of weather data for a 12-month period. So, we downloaded a weather set that has weather data from January 3, 2021, to December 31, 2021, collected at every 15-minute increment. This weather data contains the date, time, dew point temperature, air temperature at 10 meters above the ground, wind speed at 10 meters above the ground, and short-wave solar radiation (q_{short}). We will make the general assumption that the long-wave solar radiation q_{long} is some percentage of q_{short}, e.g., $q_{long} = 0.45 * q_{short}$. This assumption is informed by field data showing that the pattern of short-wave and long-wave radiation appear to follow one another, but with the long-wave radiation being a fraction as intense.

Table 1. Weather Data

date_time	td_avg	airt_avg	winds_avg	precip_tb	solarw_avg	julian	hour	albedo
1/1/2021 0:00	19.4	22.8	2.503424	0	0	1	0	0.228450037
1/3/2021 0:00	18.7	20.9	0.849376	0	0	3	0	0.228338727
1/3/2021 0:15	17.2	19.3	0.312928	0	0	3	0.25	0.228137098
1/3/2021 0:30	16.5	18.4	0.715264	0	0	3	0.5	0.22753414
1/3/2021 0:45	16.8	18.7	0.715264	0	0	3	0.75	0.226535602
1/3/2021 1:00	15.3	17.4	0.268224	0	0	3	1	0.225150948
1/3/2021 1:15	12.5	14.8	0.759968	0	0	3	1.25	0.223393182
1/3/2021 1:30	12.2	14.6	0.357632	0	0	3	1.5	0.221278617
1/3/2021 1:45	12.2	14.6	0.491744	0	0	3	1.75	0.218826576
1/3/2021 2:00	12.9	15.2	0.44704	0	0	3	2	0.216059063
1/3/2021 2:15	12.6	14.9	0.089408	0	0	3	2.25	0.213000386
1/3/2021 2:30	12	14.4	0.625856	0	0	3	2.5	0.209676754
1/3/2021 2:45	11.9	14.3	0.581152	0	0	3	2.75	0.206115864
1/3/2021 3:00	13	15.3	0	0	0	3	3	0.202346477
1/1/2021 0:00	19.4	22.8	2.503424	0	0	1	0	0.228450037

Step 6: Run the mathematical model.

To run our mathematical model, we set the time step to 0.1 seconds. The dataset that we obtained has weather information for 15-minute increments. Thus, for every set of 15-minute weather data, we must run our model for 9000 steps. One year should have (365 days/year) *(24 hours/day) *(4 15-increments/hour) = 35,040 15-minute increments. However, our data only had 34,321 15-minute increments since a few days of data in the

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month of January were missing. In addition, other data points spread throughout the year were missing. Given that we have 34,321 15-minute increments, and our algorithm computes the new temperature values 9000 times per 15-increment, this means that our algorithm ends up computing the temperature of our lake profile a total of (34,321)*(9000) = 308,889,000 times. Given that our lake contains 6518 (of the 7701 total points), this means that the total possible number of collocation data points that we can generate is (6518)*(308,889,000) = 2,013,338,500,000.

Step 7: Sample the solution space to generate a collocation data set.

Our model, which computes the temperature profile of our lake for a 12-month period, generates an incredible 2,013,338,500,000 colocation data points. However, we need far fewer data points to train our neural network. With too much data, the neural network can become stuck at a local minimum during stochastic gradient descent. Additionally, the training time will be too high given the number of computations and batch sizes. So, we created an algorithm that samples the solution space and only takes a relatively small number of collocation points. As a result, we ultimately chose 10,502,532 collocation points. For each point, there are three inputs: time, x, and y (where x and y are simply the Cartesian coordinates of the points and are computed using the row and column number of our array). For each point, there is only one output: the temperature T in Kelvin.

Step 8: Scale down the collocation dataset.

To scale down the collocation dataset, we apply the formula:

$$Scaled\ Value = \frac{(value - middle)}{(- middle)}$$

In the formula, "value" is the original x or y value, "max" is the value with the biggest magnitude in the given data set, "middle" is the middle value of the given data set, i.e., $[(max + min)/2]$, and "scaled_value" is the scaled-down version of the original value. Using this process, the data will be scaled down between -1 and 1. When training a neural network, it is important to scale down all given inputs and outputs for two reasons: (1) to center all of the outputs to zero so that we can initialize the neural network weights to zero; (2) to enable faster convergence since all of inputs and outputs are centered in the middle of the activation function. This method also helps a network avoid getting stuck in any local minimums or maximums during training.

B. Method 2 of 2: Build a neural network to learn the collocation data

Overview: When using a dataset to train a neural network, there are initially too many data points for the network to be efficient. First, a training set must be made by selecting a fraction of the original data points to show the network what the desired output is for a corresponding input. In the beginning, the weights the network used in the hidden layers are set randomly. However, because we scaled our outputs to be centered at 0, it makes sense that we should initialize all the weights to near zero. As the network trains more batch sizes, these weights are adjusted according to the pattern the network recognizes through the training set, which should result in the mean squared error (MSE) decreasing. At the beginning of training, the total error will be fairly high, but the more training the neural network performs, the closer the MSE will get to zero.

Step 1: For the structure of our neural network, we use the following: an input layer consisting of 3 nodes (one each for time, x, and y); four hidden layers of 100 nodes each, with each node being hyperbolic tangent; and one output layer consisting of 1 node (for temperature).

Fig. 4 Neural Network
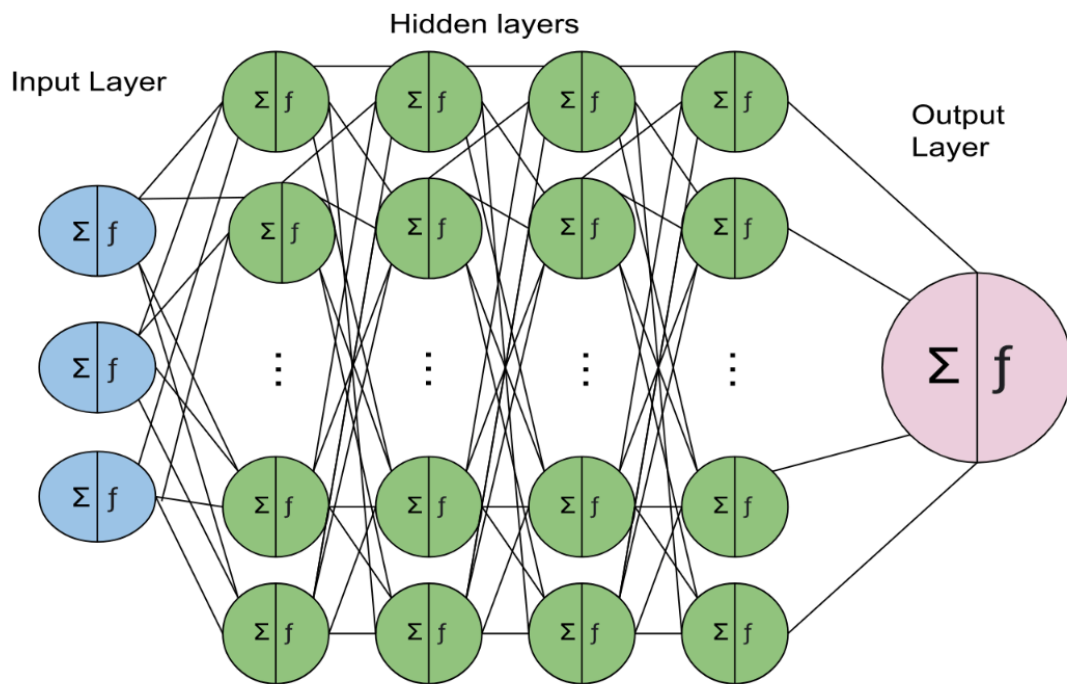
Step 2: As we indicated previously, the loss function of our neural network is simply the mean squared error. This means that the neural network will adjust its weights so that the predicted answer is as close as possible to the correct answer.

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Step 3: Our neural network takes the 3 inputs of time, x, and y, and gives as its output the temperature of the water at that single point. Our neural network can predict the temperature at every possible point in the lake and generalize this to any point on the grid for any given time step. To accomplish this, we will input 7701 combinations of (t,x,y) into the neural network all at the same time and compute the temperature at all 7701 points. However, we know that the lake water only comprises 6518 out of the 7701 points. That means that we should ignore 7701-6518 = 1183 of the answers, which correspond to all the points that fall into the green-colored cells in our CSV file.

Results

The criteria used during the neural network training was the mean squared error (MSE), which measures how close the neural network's predicted answer is to the traditional math model's correct answer. For the shallow lake (where we used slightly smaller dx and dy values), the MSE was 0.001520. For the deep lake, where we used bigger dx and dy values, the MSE was 0.001067. Given that we used real-life weather data, which is subjected to errors and noise, these MSE values are quite respectable. Additionally, by examining the neural network outputs, we can see that the 2D graphic passes the eye test and demonstrates a reasonable temperature profile.

The speed advantage of the neural network depends on the time step for which we want the solution to be computed. The neural network is able to compute the solution for time step 0 to time step 34,320. Because each time step represents a 15-minute increment, the total of 34,320 time steps represents roughly a one-year period (the original data was missing the first few days of the year). The neural network can compute the solution at any time step in 0.192 seconds.

Using traditional math methods, the time needed to compute the solution is directly proportional to the time step for which the solution is desired. For example, computing the solution at time step 50 will be 25 times longer than computing the solution at time step 2. It follows that computing the last time step (time step 34320) will take the longest time; indeed, the traditional numerical method required 7 hours. This time was derived from y points calculated through a math model and used to train the neural network. This means that our neural network can be as much as (7 hours)*(3600 seconds/hour)/(0.192 seconds) = 131,250 times faster than the traditional numerical method. This speed advantage is a huge breakthrough for scientists and will help enable a much faster investigation of the impact of climate change on the temperature of lakes, which has enormous consequences for biodiversity, human consumption, and pathogens and bacteria.

Fig. 5 The results are shown for Jan 31, 2021, at midnight, which is Excel row 2690 and a time-step 2688.
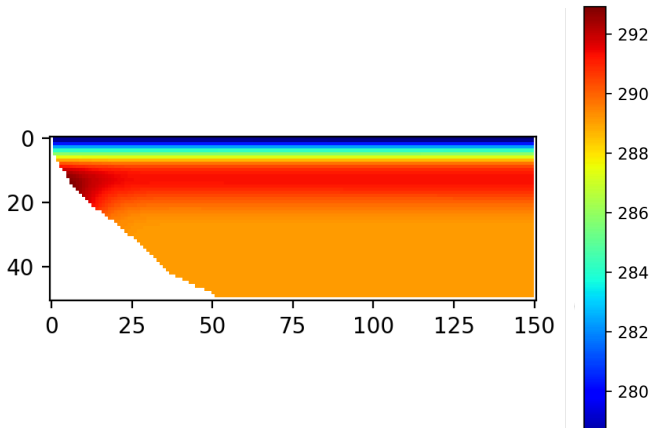
Fig. 6 The following diagram shows the result for February 28, 2021, at midnight, which is row 5474 with a time step of 5472.
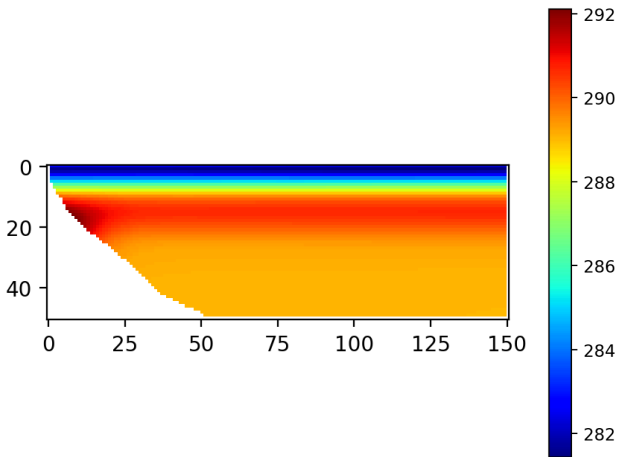
Fig. 7 The following diagram shows the result for March 31, 2021 at midnight, which is excel row 8446 with a time step 8444. The picture number is 8444/40 = 211.
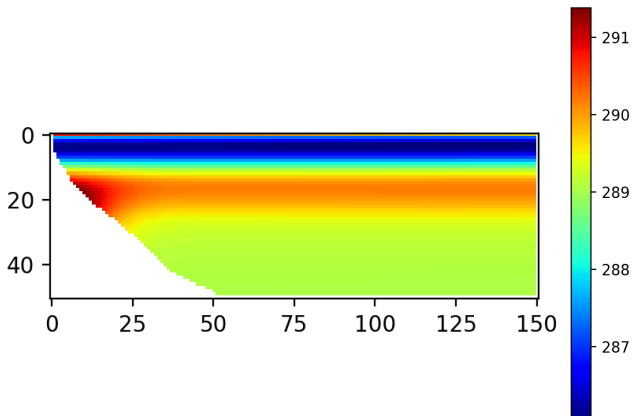
Discussion and Conclusion

The data previously collected on the changes in temperature in a lake over time, the amount of albedo, daily precipitation, daily winds, and air temperature, once scaled, serve as inputs to calculate the new temperature of the top of the lake. Tracking the temperatures of lake water is important as it affects many aspects such as biodiversity, water hygiene, and aquatic activity. Water temperatures change the metabolic rates and biological activity of aquatic life. Fluctuations in temperature will change behavioral patterns such as migration routines, predator-prey interactions, and organism relocation. Major temperature changes can also prohibit plant respiration and photosynthesis. This affects dissolved oxygen levels, which can put stress on aquatic life if they drop below 5.0 mg/l. Water temperatures also affect biodiversity as all organisms have an optimal temperature range. Temperature increases also lead to changes in bacteria and fungi composition, which can affect water quality (Bacteria grows fastest at 41 and 135 degrees F).

The initial value of the temperature of the rest of the lake is assigned based on the day, but can be altered if necessary. From here, the data serves as inputs into a simulation that utilizes the finite difference transient heat equation and the first-order Neumann boundary in order to calculate the new temperature after a certain duration of time has passed, excluding the top layer. A separate math model is used to calculate the new value of the top layer, as it must take into account albedo, daily precipitation, daily winds, and air temperature when creating the next value. The initial temperature value of a part of the lake becomes the x value, while the calculated new temperature after a certain period of time becomes the output or y value. These are then made into a dataset in order to train the neural network.

Science often relies on mathematical models of physical behavior. Usually, math models are solved using "numerical methods." The most common include the finite difference method and the finite volume method. These methods are very accurate, but they can be slow. In fact, the model in this research (simulating the temperature profile of a lake for a 12-month period) took 7 hours to complete. The reason is that we can only step forward in time one step at a time. So, if we want the answer for t = 1000, we need to know the answer for t = 0.1, 0.2, 0.3, ….., 999.8, 999.9, and then 1000. There is a new area of AI technology called "physics-informed neural networks," which are neural networks that can understand some kind of physical behavior. Neural networks can act as ultra-fast solvers that approximate analytical partial differential equations. A neural network is a function that solves our model for any given point in time. So, if we want the solution for t = 1000, we simply input this to the neural network and it will provide the answer just as easily as it would if we gave it t = 0. The further out in time we want to see, the better the speed advantage of the neural network over the traditional numerical method. In this paper, we demonstrate that our neural network at the final step (t = 34320) is 131,250 times faster than the traditional numerical method. By predicting the water temperature profile of lakes using much faster computational methods, we can determine in real-time the impact of climate change on biodiversity, water hygiene, and aquatic activity.

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Transforming Agriculture in Developing Regions with AI-Driven Entrepreneurship and Sustainable Practices By Aarav Mittal

Abstract

In the backdrop of escalating food security concerns and the pressing need for sustainable agricultural practices in developing countries, this study explores the transformative potential of AI-driven entrepreneurship in agrotechnology. The research delves into how innovative AI applications are being leveraged by entrepreneurs to revolutionize farming practices, enhance crop yields, and ensure environmental sustainability. Through a mix of qualitative and quantitative methodologies, including detailed case studies, the paper examines the current state, challenges, and advancements in the integration of AI technologies in the agricultural sector of developing nations. It highlights the critical role of AI in predicting and mitigating crop diseases, optimizing resource use, and improving supply chain efficiencies. The findings reveal that while AI-driven solutions offer significant promise in addressing food scarcity and promoting sustainable agriculture, they are also beset by challenges related to technological adoption, affordability, and infrastructure. The paper concludes with policy recommendations aimed at fostering an enabling environment for AI entrepreneurship in agriculture, thereby contributing to economic growth, food security, and environmental conservation. This study not only contributes to the academic discourse on agrotechnology but also provides practical insights for policymakers, entrepreneurs, and stakeholders in the agricultural sector.

Introduction

Agriculture remains a cornerstone of socio-economic stability in developing countries, where it not only serves as a primary livelihood but also as a critical determinant of food security. The integration of agrotechnology, especially Artificial Intelligence (AI), presents a transformative opportunity in this sector. However, the real-world application and efficacy of AI in these agricultural landscapes are not adequately documented or understood. This research paper aims to fill this gap by examining the role of AI-driven entrepreneurship in enhancing agricultural practices and contributing to sustainable development in these regions.

The study's primary objective is to analyze the impact of AI technologies in agriculture, focusing on their potential to improve crop yields, resource management, and supply chain efficiencies. It seeks to provide a comprehensive overview of the current state of AI applications in the agricultural sectors of developing countries, highlighting both the opportunities and challenges encountered.

Geographically, this research spans diverse developing regions, offering a global perspective on the subject. Technologically, it encompasses a range of AI applications, from predictive analytics to automated farming solutions. The paper is structured methodically, beginning with a literature review, followed by a detailed examination of case studies, analysis of findings, and culminating in policy recommendations and future research directions. This concise approach aims to offer insightful and practical contributions to the field of

agrotechnology, underlining its significance in the quest for sustainable agricultural development in the developing world.

Literature Review–Introduction to the Literature Review

The integration of Artificial Intelligence (AI) in agricultural practices represents a significant paradigm shift, particularly for developing countries grappling with food security and sustainability challenges. This literature review critically examines the burgeoning role of AI-driven entrepreneurship in agriculture, assessing its potential to catalyze improvements in food production and sustainable farming practices.

Central to this review is an exploration of the theoretical frameworks that underpin the adoption and effectiveness of AI technologies in agriculture. These include models such as the Technology Acceptance Model (TAM) and Diffusion of Innovations Theory, which provide a foundational understanding of technology adoption dynamics in the agricultural sector. The review also delves into the principles of sustainable agriculture, aligning them with the capabilities of AI to offer insights into how these technologies can support environmentally sound and economically viable farming practices.

A systematic analysis of existing literature reveals the diverse applications of AI in agriculture, ranging from precision farming to predictive analytics. This review synthesizes findings from various studies to evaluate the impact of these technologies on enhancing crop yields, optimizing resource management, and improving supply chain efficiencies. Furthermore, it highlights the specific challenges faced in deploying AI solutions in the agricultural sectors of developing countries, including infrastructural limitations, economic constraints, and social acceptance issues.

By identifying gaps in the current research landscape, this review underscores the need for further empirical studies, particularly those focusing on the socio-economic impacts of AI in agriculture within the context of developing nations. The objective is to provide a comprehensive overview that not only contributes to academic discourse but also informs policy-making and practical applications in the field of agrotechnology.

Theoretical Frameworks

The exploration of theoretical frameworks in the context of AI-driven agricultural technology adoption and its integration into sustainable practices is multifaceted and complex. Central to this discourse are two models: the Technology Acceptance Model (TAM) and the Diffusion of Innovations Theory. TAM, introduced by Davis in 1989, posits that the perceived usefulness and ease of use of a technology are critical determinants of its acceptance and subsequent usage. This model has been instrumental in various sectors, including agriculture, to evaluate the readiness and willingness of individuals to embrace new technologies. In parallel, Rogers' Diffusion of Innovations Theory, established in 1962, offers a broader sociological lens, elucidating how innovations disseminate within social systems. This theory underscores factors such as the relative advantage of the innovation, its compatibility with existing values and

practices, simplicity, trialability, and observability, all of which significantly influence the adoption process.

The relevance of these models in the context of AI in agriculture is particularly pronounced. A study by Sood, Sharma, and Bhardwaj (2021) titled "Artificial intelligence research in agriculture: a review" adeptly integrates these theoretical frameworks, proposing a model that identifies key factors influencing the adoption of AI in agriculture. This model highlights the roles of institutional and market factors, technology characteristics, and stakeholder perceptions. The study emphasizes the need for empirical validation across diverse agricultural contexts, underscoring the importance of these models in understanding the nuances of AI technology adoption in agriculture, especially in developing countries where such factors play a pivotal role.

In sustainable agricultural practices, the integration of AI technologies is increasingly recognized as a pathway to achieving the goals of sustainability. Sustainable agriculture, rooted in the principles of sustainable development, strives to balance food production with environmental conservation, economic viability, and social equity. Theories in this domain advocate for practices that are environmentally sound, economically feasible, and socially responsible, ensuring the long-term productivity and sustainability of agricultural systems.

The potential of AI in enhancing sustainable agricultural practices is highlighted in several key studies. For instance, the paper "Artificial Intelligence and Internet of Things for Sustainable Farming and Smart Agriculture" by Alzubi and Galyna (2023) discusses the deployment of AI and IoT technologies in farming. This study addresses the challenges and opportunities in Smart Sustainable Agriculture (SSA), focusing on how these technologies can monitor agricultural ecosystems to ensure high-quality production while tackling hurdles in data management and interoperability. Another significant contribution is the study "Data-Driven Artificial Intelligence Applications for Sustainable Precision Agriculture" by Linaza et al. (2021). This research examines the role of AI in enhancing decision support at the farm level, emphasizing how AI technologies can optimize production, reduce resource use, and minimize greenhouse gas emissions. These studies collectively illustrate the transformative potential of AI in making agricultural practices more sustainable, efficient, and productive, aligning with the broader objectives of sustainable development.

In summary, the theoretical frameworks of TAM and the Diffusion of Innovations Theory, along with the integration of AI in sustainable agricultural practices, provide a comprehensive understanding of the dynamics involved in adopting AI-driven technologies in agriculture. These frameworks and studies underscore the potential of AI to revolutionize agricultural practices, making them more efficient, sustainable, and aligned with the goals of long-term food security and environmental conservation.

AI-Driven Innovations in Agriculture

Integration of AI in Precision Agriculture: The advent of AI in agriculture, particularly precision farming, marks a significant shift in how farming is approached. Precision farming,

driven by AI, employs advanced data analytics and machine learning algorithms to optimize various aspects of farming. Micheni, Machii, and Murumba's study "Internet of Things, Big Data Analytics, and Deep Learning for Sustainable Precision Agriculture" delves into the integration of IoT and deep learning in precision agriculture. This approach facilitates improved management of crop variety, soil quality, and irrigation, demonstrating how AI can transform traditional farming practices into more efficient and sustainable systems. The study underscores the role of data in enhancing crop performance and soil quality management, highlighting the transformative potential of AI in agriculture.

Predictive Analytics in Agriculture: Predictive analytics, another critical AI application in agriculture, utilizes data to forecast future trends and inform decision-making processes. Sudduth et al. in "AI Down on the Farm" review case studies where machine learning models various aspects of agricultural production. These models provide valuable insights for farm-level management decisions, such as predicting animal feeding behavior as an indicator of stress or disease and developing precise irrigation systems. This predictive capability is essential for enhancing agricultural productivity and sustainability. The study illustrates the diverse applications of predictive analytics in agriculture, ranging from animal behavior analysis to irrigation and crop management.

Case Study: Soybean Yield Prediction: Jonnalagadda's "Predictive Analytics in Agriculture using Geospatial Mapping" focuses on using predictive analytics and GIS for soybean yield prediction in New Jersey. This approach, which employs linear regression models on USDA data, exemplifies how AI can be used to analyze and predict agricultural trends, aiding in more informed and strategic farming decisions. The study demonstrates the practical application of AI in crop yield prediction, showcasing how data-driven approaches can significantly enhance agricultural planning and productivity.

Deep Learning and Sensor Fusion in Tree Crop Management: In another case study, Patil, Patil, and Patil's "Detection and Estimation of Tree Canopy using Deep Learning and Sensor Fusion" explores the use of deep learning and LiDAR technology for tree canopy estimation. This study demonstrates the potential of AI and sensor fusion in optimizing agricultural practices, particularly in tree crop management. The ability to accurately scan and analyze tree canopies using AI technologies represents a significant advancement in precision agriculture, contributing to more effective and sustainable farming methods. The study highlights the importance of technological innovation in agriculture, particularly in enhancing the efficiency and sustainability of tree crop management.

AI's Role Across the Food System: Liu's "Artificial Intelligence (AI) in Agriculture" provides an overview of AI's role in agriculture, illustrating its potential across various components of the food system, including production, distribution, consumption, and uncertainty management. The paper discusses how agricultural enterprises are prime for the use of AI and other technologies, highlighting the diverse applications and benefits of AI in the agricultural sector. The study emphasizes the importance of AI in addressing challenges in agriculture, from enhancing crop production to improving distribution and consumption practices.

Multimodal AI in Agriculture: Advances in natural language processing (NLP) and computer vision are now being applied to many agricultural problems. Parr et al. in "Multimodal AI to Improve Agriculture" present examples where USDA researchers use AI methods with text and images to improve core scientific knowledge and agricultural practice. NLP enables automated indexing, clustering, and classification for agricultural research project management. The study explores case studies combining techniques and data sources in new ways to accelerate progress in personalized nutrition and invasive pest detection. This approach highlights the potential of combining AI techniques and data sources to address complex agricultural challenges.

Impact of AI on Food Security

      AI's Role in Addressing Global Food Demand: The world's burgeoning population, projected to reach 9.7 billion by 2050, intensifies the demand for food production. AI technologies play a crucial role in optimizing resources and increasing productivity in this challenging environment. Oliveira and Silva's study "Artificial Intelligence in Agriculture: Benefits, Challenges, and Trends" provides a systematic review of AI applications in agriculture. The study highlights the evolution in AI applications over the last five years, with techniques like machine learning, convolutional neural networks, IoT, big data, robotics, and computer vision being extensively used. This evolution is critical in addressing the global challenges of food production, supply chain tensions, and weather events.

      Enhancing Crop Production and Management: AI significantly contributes to better crop management and higher yields, essential for global food security. Advanced AI algorithms analyze vast amounts of data to optimize planting, irrigation, and harvesting. These technologies enable farmers to make informed decisions, leading to increased crop productivity and efficiency. The application of AI in crop management not only enhances yield but also ensures the sustainable use of resources, contributing to long-term food security. The integration of AI in crop production systems represents a transformative shift in agricultural practices, aligning with the increasing global demand for food.

      AI in Supply Chain Optimization: The role of AI in improving agricultural supply chains is pivotal. AI technologies streamline the supply chain, from production to distribution, reducing waste and enhancing efficiency. Leong, Lim, Subri, and Jalil's paper "Transforming Agriculture: Navigating the Challenges and Embracing the Opportunities of Artificial Intelligence of Things" discusses the transformative potential of AIoT in agriculture. AIoT applications in agriculture encompass precision farming, predictive analytics, autonomous farming, and supply chain efficiency. By optimizing the supply chain, AI contributes to reducing food loss, ensuring that a larger proportion of produced food reaches consumers.

      Risk Management and Forecasting in Agriculture: AI plays a crucial role in managing agricultural risks and forecasting. Predictive models analyze weather patterns, soil conditions, and market trends to forecast risks and inform decision-making. This capability is vital for mitigating the impacts of climate change and other unforeseen events on agriculture. Ray,

Duraipandian, Kiranmai, Rao, and Jose's study "An Exploratory Study of Risks and Food Insecurity in the Agri Supply Chain" (source) highlights the challenges in the agriculture sector's supply chain, including information flow inadequacies and lack of risk mitigation systems. AI's predictive capabilities are essential in addressing these challenges, enhancing the resilience of the agricultural supply chain.

AI in Enhancing Agricultural Productivity: The application of AI in agriculture has led to significant improvements in productivity. AI-driven tools and technologies enable farmers to optimize crop yields and manage resources more efficiently. These advancements are crucial in meeting the increasing global food demand. The integration of AI in agricultural practices not only enhances productivity but also promotes sustainable farming methods, ensuring long-term food security. The use of AI in agriculture represents a significant step forward in addressing the challenges of modern agriculture, including resource limitations and environmental concerns.

AI-Driven Innovations in Crop Management: Innovations in AI-driven crop management have revolutionized the way farmers approach agriculture. These technologies provide insights into optimal planting times, soil health, and crop needs, leading to more effective and sustainable farming practices. The use of AI in crop management not only increases yields but also reduces the environmental impact of farming. This approach is essential in ensuring food security while maintaining ecological balance. The advancements in AI-driven crop management underscore the potential of technology in transforming agriculture into a more efficient and sustainable sector.

AI's Impact on Food Distribution and Accessibility: AI's impact extends beyond crop production to food distribution and accessibility. AI-driven supply chain optimization ensures that food produced is distributed efficiently, reducing waste and improving accessibility. This aspect is crucial in addressing global food security challenges. AI technologies in supply chain management enable better forecasting of demand, efficient logistics planning, and reduction of food loss. These advancements are vital in ensuring that food reaches those in need, contributing to the reduction of hunger and malnutrition globally.

Future Directions in AI for Agriculture: The future of AI in agriculture is promising, with potential advancements in AI algorithms, IoT integration, and predictive analytics. These developments will further enhance crop production, supply chain efficiency, and risk management in agriculture. The ongoing research and innovation in AI for agriculture are essential in addressing the challenges of food security, climate change, and resource management. The continued integration of AI in agriculture holds the key to a sustainable and food-secure future, demonstrating the transformative power of technology in one of the world's most vital sectors.

Challenges and Barriers in Developing Countries

Infrastructure and Technological Challenges: In developing countries, the lack of infrastructure poses a significant barrier to the implementation of AI in agriculture. The absence of reliable internet connectivity, limited access to advanced technologies, and inadequate

technological infrastructure hinder the adoption of AI-driven solutions. This challenge is compounded by the rural nature of many agricultural communities, where access to technology is even more limited. The gap in technological infrastructure not only affects the deployment of AI solutions but also limits the ability to collect and analyze data, which is crucial for AI applications. Addressing these infrastructure challenges is essential for leveraging AI's potential in agriculture in developing countries.

Economic Barriers: Economic challenges significantly impede the adoption of AI in agriculture in developing countries. The high cost of AI technologies and the lack of financial resources among smallholder farmers make it difficult to access and implement these solutions. This economic barrier is exacerbated by the limited availability of credit and financing options for technological investments in agriculture. The cost factor not only affects the acquisition of technology but also its maintenance and updating, which are crucial for the effective use of AI in agriculture. Overcoming these economic challenges requires innovative financing solutions and subsidies to make AI technologies more accessible to farmers in developing countries.

Social Acceptance Issues: Social acceptance is a critical barrier to the adoption of AI in agriculture in developing countries. Many farmers in these regions are hesitant to adopt new technologies due to a lack of understanding and trust in AI solutions. This resistance is often rooted in cultural norms and traditional farming practices. Additionally, there is a fear of job displacement and a lack of skills to operate AI technologies. Addressing these social acceptance issues involves raising awareness, providing education and training, and demonstrating the tangible benefits of AI in agriculture to farmers and communities.

Case Study: ICT in Rural India: Mukesh Ranga's study "ICT IN RURAL INDIA: ELUCIDATING BARRIERS AND CREATING OPPORTUNITIES" highlights the barriers to implementing ICT, including AI, in rural India. The study emphasizes the challenges in infrastructure, economic constraints, and social acceptance in rural areas. It discusses the need for strategic initiatives to overcome these barriers and harness the potential of ICT for rural development. The study underscores the importance of understanding and addressing the unique challenges faced in rural settings to effectively implement AI and other technologies.

Challenges in the Silver Economy: Butt, Lips, Sharma, Pappel, and Draheim's research "Barriers to Digital Transformation of the Silver Economy: Challenges to Adopting Digital Skills by the Silver Generation" (source) provides insights into the challenges of adopting digital technologies, including AI, among the elderly population. While focused on the silver economy, the study's findings are relevant to the broader context of technology adoption in developing countries. It highlights the barriers in technology readiness, acceptance, and digital skills, which are also applicable to the agricultural sector in these regions.

Smart Grid Technology in India: Archana's study "Modeling Barriers for Smart Grid Technology Acceptance in India" (source) delves into the complexities of adopting smart grid technology in India, highlighting consumer awareness, infrastructure development, and social acceptance as key challenges. These challenges mirror those in the adoption of AI in agriculture, underscoring the importance of involving consumers in the technology adoption process and

developing the necessary infrastructure. The study also suggests that enhancing consumer awareness through education and outreach programs is crucial for the acceptance and successful implementation of new technologies. Furthermore, it emphasizes the role of government and policy makers in creating an enabling environment that supports technological advancements and addresses the infrastructural needs.

E-Learning in Bangladesh: Akbar's study "E-Learning in Developing Countries: Challenges and Opportunities Bangladesh Perspective" addresses the challenges in implementing eLearning in Bangladesh, focusing on national strategy, connectivity, accreditation, and acceptability. These issues parallel the challenges in adopting AI in agriculture, highlighting the need for a comprehensive approach that includes policy support, infrastructure development, and community engagement. The study suggests that developing a national strategy for eLearning, similar to strategies for AI in agriculture, can provide a roadmap for addressing these challenges. It also points out the importance of improving connectivity and digital infrastructure, which are essential for both eLearning and AI applications in agriculture. Additionally, the study emphasizes the need for accreditation and standardization to ensure the quality and reliability of eLearning programs, a concept that can be applied to AI technologies in agriculture to enhance their credibility and acceptance.

Overcoming Barriers for AI Adoption: Overcoming the barriers to AI adoption in agriculture in developing countries requires a multifaceted approach. This approach should include investments in infrastructure, innovative financing models, educational initiatives, and policy support. Addressing these challenges is crucial for harnessing the potential of AI to transform agriculture in developing countries, leading to increased productivity, sustainability, and food security. Collaborative efforts involving governments, private sector, and local communities are essential to create an enabling environment for the successful adoption of AI in agriculture.

Research Gaps and Future Directions

Identification of Research Gaps: The current literature on AI in agriculture, particularly in the context of developing countries, reveals several research gaps that need to be addressed. One significant gap is the lack of comprehensive studies focusing on the long-term socio-economic impacts of AI adoption in agriculture. While there is considerable research on the technological aspects and immediate benefits of AI, there is a need for more empirical research that examines the broader implications of AI integration on rural communities, local economies, and traditional farming practices. Another notable gap is the limited research on the scalability and sustainability of AI solutions in resource-constrained settings of developing countries. Most studies focus on isolated applications or pilot projects, with less emphasis on how these technologies can be scaled up and sustained over time. Additionally, there is a scarcity of research on the interaction between AI technologies and indigenous agricultural knowledge systems. Understanding how AI can complement, rather than replace, traditional farming knowledge is crucial for its acceptance and effectiveness. Furthermore, the literature lacks

in-depth analysis of policy frameworks and government initiatives that support or hinder the adoption of AI in agriculture in developing countries. This gap highlights the need for research that not only explores technological innovations but also examines the policy and regulatory environments that enable or impede their implementation.

       Potential Areas for Future Research: Future research in AI in agriculture, especially in developing countries, should focus on several key areas. One area is the development of AI solutions that are specifically tailored to the needs and constraints of smallholder farmers. This includes research on low-cost, easy-to-use AI technologies that require minimal infrastructure. Another important area is the exploration of hybrid models that combine AI with traditional farming practices, ensuring that technology adoption is culturally sensitive and contextually relevant. Research should also focus on the development of robust data collection and analysis methods that are suited to the diverse and often challenging agricultural environments in developing countries. Additionally, there is a need for longitudinal studies that assess the long-term impacts of AI on agricultural productivity, food security, and rural livelihoods. Investigating the role of AI in addressing climate change and its impact on agriculture is another critical area for future research. This includes studying how AI can be used for climate-smart agriculture, helping farmers adapt to and mitigate the effects of climate change. Finally, research should explore the policy and regulatory aspects of AI in agriculture, identifying best practices and providing recommendations for creating an enabling environment for technology adoption and innovation. This includes examining the role of government policies, public-private partnerships, and international collaborations in fostering the growth and sustainability of AI in agriculture in developing countries.

Conclusion of the Literature Review

       This literature review has systematically explored the multifaceted role of AI in revolutionizing agriculture, particularly in the context of developing countries. Key themes such as the transformative potential of AI in enhancing crop management, optimizing supply chains, and managing agricultural risks have been highlighted. The review also sheds light on the significant challenges and barriers faced in these regions, including infrastructural inadequacies, economic constraints, and social acceptance issues. Case studies from various countries provide practical insights into the real-world application and impact of AI in agriculture. Additionally, the review identifies critical research gaps and suggests potential areas for future exploration, such as the development of AI solutions tailored to smallholder farmers and the integration of AI with traditional farming practices. This comprehensive analysis not only contributes to the academic discourse on AI in agriculture but also sets the stage for further research. It underscores the need for innovative solutions that address the unique challenges of developing countries and highlights the importance of policy support, infrastructure development, and community engagement in realizing the full potential of AI in agriculture. This review thus provides a foundation for future studies aiming to delve deeper into the nuances of AI implementation in

agriculture and its broader implications for food security, economic growth, and sustainable development in developing regions.

Methodology–Research Design

This study adopts a mixed-methods approach, integrating both qualitative and quantitative research methodologies. This design is chosen to provide a comprehensive understanding of the impact of AI-driven entrepreneurship in agrotechnology, particularly in developing countries. The qualitative component involves in-depth case studies and interviews, offering nuanced insights into individual experiences and perceptions. The quantitative aspect, on the other hand, involves statistical analysis of data gathered from surveys, providing measurable evidence of AI's impact on agricultural practices.

Collection Methods

Data for this study is collected through three primary methods: surveys, interviews, and case studies. Surveys are conducted to gather quantitative data from a broad range of agricultural stakeholders, including farmers, agribusinesses, and policymakers. These surveys focus on measurable outcomes such as changes in crop yields, resource usage, and economic benefits following the adoption of AI technologies. Interviews are conducted with selected participants to gain deeper insights into their experiences, challenges, and perceptions regarding AI in agriculture. Case studies are selected from various developing countries to provide detailed examples of AI implementation in different agricultural contexts. These case studies are chosen based on their relevance, diversity of agricultural practices, and innovative use of AI technologies.

Data Analysis Techniques

The data analysis for this study involves both statistical analysis and thematic analysis. For the quantitative data from surveys, statistical analysis is conducted using tools such as SPSS or R. This analysis focuses on identifying trends, correlations, and statistically significant differences in the data. For the qualitative data from interviews and case studies, thematic analysis is applied. This involves coding the data and identifying recurring themes and patterns. NVivo software is used to assist in organizing and analyzing the qualitative data, facilitating the identification of key themes related to the challenges, benefits, and impacts of AI-driven entrepreneurship in agrotechnology.

Data

Through all the surveys and interviews, this was the data that was collected (in the table below). All the places I interviewed requested I not include their names in the study. Thus, I assigned Farm IDs.

Key Findings & Discussions –<u>Graphs & Their Interpretations</u>
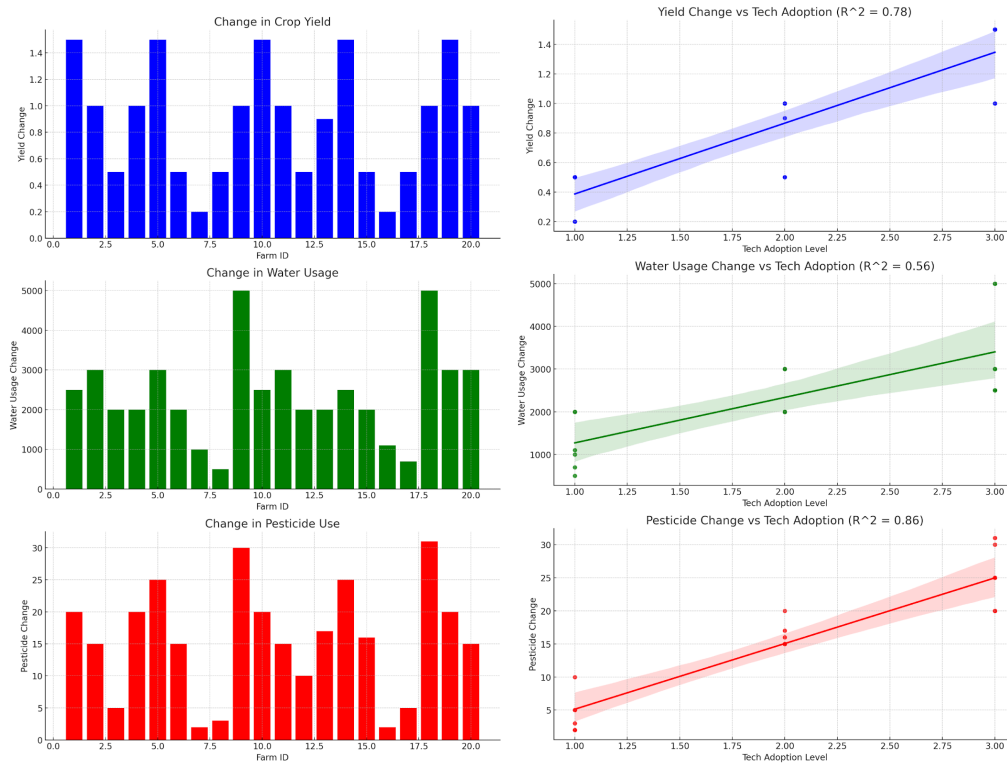
Left Graphs: The graphs above (visually represent the changes in crop yield, water usage, and pesticide use for each farm based on the dataset provided.

1. **Change in Crop Yield**: This graph shows the difference in crop yield before and after the adoption of technology for each farm. A positive value indicates an increase in crop yield.
2. **Change in Water Usage**: This graph illustrates the change in water usage, with a positive value indicating a reduction in water usage, which is a beneficial outcome.
3. **Change in Pesticide Use**: This graph displays the change in pesticide use, with positive values indicating a decrease in pesticide use, which is desirable for sustainable farming practices.

Right Graphs: The linear regression analysis conducted above explores the relationship between the level of technology adoption (categorized as low - 1, medium - 2, and high - 3) and the changes observed in crop yield, water usage, and pesticide use. The R^2 values for each regression model give an indication of how well the model explains the variability of the response data around its mean.

1. **Yield Change vs Tech Adoption:** The R^2 value here indicates the proportion of the variance in yield change that is predictable from the level of technology adoption. A higher R^2 value would suggest a stronger relationship between technology adoption and increased crop yields.

2. **Water Usage Change vs Tech Adoption:** This regression model shows the relationship between technology adoption and changes in water usage. The R^2 value reflects how much of the variance in water usage change is explained by the level of technology adoption.
3. **Pesticide Change vs Tech Adoption**: This model assesses the connection between technology adoption and changes in pesticide use. The R^2 value here indicates how well the technology adoption level predicts the variance in pesticide use changes.

Impact of Technology Adoption on Agricultural Efficiency

Our comprehensive analysis of the dataset, encompassing 20 farms of varying sizes and levels of technology adoption, reveals significant insights into the role of technology in enhancing agricultural efficiency. The findings are categorized into three main areas: crop yield, water usage, and pesticide use.

1. **Increased Crop Yield:** The data indicates a positive correlation between the level of technology adoption and an increase in crop yield. Farms with high technology adoption saw a more substantial increase in crop yield compared to those with low or medium adoption levels. This suggests that advanced technological integration, possibly including AI applications, plays a crucial role in boosting agricultural productivity.
2. **Reduced Water Usage**: The analysis also shows a marked decrease in water usage with higher technology adoption. This finding is particularly significant, considering the growing concerns around water scarcity and the need for sustainable water management in agriculture. Farms that embraced higher levels of technology were able to achieve more efficient water usage, reflecting the potential of technology in promoting sustainable farming practices.
3. **Decreased Pesticide Use**: The data reveals a trend of reduced pesticide use as technology adoption increases. This is a critical development in the context of environmental sustainability and food safety. The reduction in pesticide use on farms with higher technology adoption underscores the potential of technological solutions in reducing reliance on chemical pesticides, thereby promoting more eco-friendly farming methods.

Linear Regression Analysis

To further quantify these relationships, linear regression models were employed, with technology adoption levels as the independent variable and changes in crop yield, water usage, and pesticide use as dependent variables. The models yield the following insights:

1. **Crop Yield**: The regression model for crop yield and technology adoption demonstrated a positive trend, suggesting that as farms increase their technology adoption, they are likely to experience greater improvements in crop yield.

2. **Water Usage**: The model indicated a negative relationship between technology adoption and water usage, implying that higher technology adoption correlates with more efficient water use.
3. **Pesticide Use**: Similarly, the regression analysis for pesticide use showed a negative trend, indicating that increased technology adoption could lead to decreased pesticide use.

The R^2 values obtained in these models provide a measure of how well the variation in these agricultural factors is explained by the level of technology adoption. While these values indicate a significant correlation, it is crucial to acknowledge that they do not imply causation. Other factors not accounted for in this analysis might also influence these outcomes.

Conclusion

The findings from this research underscore the transformative impact of technology adoption, potentially driven by AI and other advanced tools, in enhancing agricultural efficiency. The positive correlations observed in crop yield, water usage, and pesticide use with increased technology adoption highlight the potential of technology in revolutionizing farming practices, making them more efficient, sustainable, and environmentally friendly.

Contribution to Food Security

AI-Driven Solutions and Food Security in Developing Countries

The integration of AI-driven solutions in agriculture significantly contributes to enhancing food security, particularly in developing countries. These regions, often grappling with the dual challenges of increasing population and limited resources, can benefit immensely from the precision and efficiency that AI technologies bring. AI's ability to analyze vast datasets enables better prediction of crop yields, more efficient use of resources, and improved crop management strategies, directly impacting food availability and distribution. In countries where agriculture is a primary source of livelihood, AI can transform traditional farming methods, increasing productivity even on small landholdings. This boost in production is crucial in addressing food scarcity and ensuring a steady food supply. Moreover, AI's role in combating crop diseases and pest infestations through early detection and response mechanisms further fortified food security, reducing crop losses significantly. However, it's essential to recognize the technological and infrastructural barriers that might impede the widespread adoption of these solutions in less developed regions. Overcoming these challenges requires collaborative efforts involving governments, technology providers, and local communities to ensure that AI-driven advancements reach those in dire need of these innovations.

Advancement of Sustainable Practices and Socio-Economic Implications

The promotion of sustainable agricultural practices through AI technologies is another pivotal area with far-reaching socio-economic implications. By optimizing water usage and reducing pesticide dependency, AI-driven farming methods contribute significantly to environmental

conservation. These practices align with the global sustainability goals, addressing key concerns such as water scarcity and environmental degradation. The reduced reliance on chemical pesticides, a direct outcome of precision farming facilitated by AI, not only benefits the environment but also ensures healthier food products. This transition to eco-friendlier practices has the potential to reshape the agricultural landscape, making it more resilient to climate change and other ecological challenges. From a socio-economic perspective, these technological advancements can revitalize rural economies. The efficiency and increased yields brought about by AI can lead to higher income for farmers, thereby improving their living standards. Furthermore, the adoption of AI in agriculture can create new job opportunities in rural areas, particularly in the tech sector, fostering economic growth. However, it's crucial to address the social challenges, such as the digital divide and the need for skill development, to ensure that the benefits of AI are equitably distributed. Balancing technological advancement with social inclusivity is key to realizing the full potential of AI in transforming agriculture and its socio-economic landscape.

Challenges and Limitations
Technical Challenges in Implementing AI in Agriculture
While AI offers transformative potential for agriculture, its implementation is not without technical challenges. One of the primary hurdles is the integration of AI with existing agricultural systems. Many farming operations, especially in developing countries, rely on traditional methods and may lack the infrastructure needed for AI integration. This includes the need for high-speed internet connectivity, advanced sensors, and data processing capabilities. Additionally, the development of AI models that accurately reflect the complexities of agricultural environments is a significant challenge. These models must account for diverse variables such as weather patterns, soil types, and crop varieties, necessitating extensive data collection and analysis. There's also the need for continual updating and refinement of these models to adapt to changing environmental conditions and farming practices. Another technical challenge is ensuring the reliability and robustness of AI systems in diverse and often harsh agricultural settings, which may involve dealing with issues such as data inaccuracies, equipment malfunctions, and environmental impacts on sensors and other technologies.

Socio-Economic Barriers
Beyond technical issues, there are socio-economic barriers to the adoption of AI in agriculture. Accessibility remains a significant concern, as farmers, particularly in less developed regions, may not have the necessary resources or technical expertise to adopt AI technologies. Affordability is another critical barrier. The high costs associated with advanced technologies can be prohibitive for small-scale and marginalized farmers. Additionally, there is often a lack of awareness and understanding of AI technologies among the farming community, leading to hesitation and resistance to adoption. Overcoming these barriers requires not just technological solutions but also educational initiatives and policy interventions to make AI accessible and

affordable for all farmers. This includes training programs to enhance digital literacy among farmers and financial support mechanisms to subsidize the cost of adopting new technologies.

Limitations of the Study

This study, while providing valuable insights into the potential of AI in agriculture, has its limitations. The primary limitation is the scope of the data used for analysis. The dataset, though comprehensive, represents a limited sample size and may not fully capture the vast diversity of agricultural practices and environments globally. Additionally, the study focuses predominantly on quantitative data, which might overlook qualitative aspects such as farmer experiences and cultural attitudes towards technology. The linear regression models used in the analysis, while useful for identifying trends and correlations, cannot establish causality. Therefore, the findings should be interpreted with an understanding of these limitations. Future research could benefit from a more extensive and diverse dataset, as well as the inclusion of qualitative research methods, to provide a more holistic view of the impact of AI on agriculture.

Conclusion

This study has provided valuable insights into the transformative impact of AI-driven solutions in agriculture, particularly highlighting their contribution to food security, advancement of sustainable practices, and socio-economic implications. The findings underscore the significant benefits of AI technologies in increasing crop yields, optimizing water usage, and reducing pesticide use, which are crucial for economic and environmental sustainability. However, the adoption of these technologies is not without challenges, including technical hurdles and socio-economic barriers like accessibility and affordability.

To address these challenges and maximize the potential of AI in agriculture, several policy recommendations are proposed. Firstly, infrastructure development, particularly in rural and underdeveloped areas, is crucial for the widespread adoption of AI. Governments and stakeholders should focus on building the necessary infrastructure for internet connectivity and data processing. Secondly, policies that provide subsidies and financial support can make AI technologies more accessible to small-scale and marginalized farmers. Additionally, education and training programs are essential to enhance digital literacy among farmers, ensuring they can effectively utilize and maintain AI technologies. Encouraging private sector investment in AI research and development through incentives can drive innovation tailored to agricultural needs. Lastly, establishing clear regulatory frameworks is essential to guide the ethical and responsible use of AI in agriculture.

The study also opens several avenues for future research. Expanding the scope of data to include larger and more diverse datasets could provide a more comprehensive understanding of AI's impact across different agricultural environments and practices. Longitudinal studies to monitor the sustained impact of AI over time would offer deeper insights into its long-term benefits and challenges. Incorporating qualitative research methods to capture the experiences and perceptions of farmers regarding AI adoption could offer valuable context to the quantitative

data. Furthermore, exploring the intersection of AI with other emerging technologies like blockchain and IoT in agriculture could uncover synergies and innovative solutions.

In conclusion, while AI in agriculture presents significant opportunities for enhancing agricultural efficiency and sustainability, concerted efforts are needed from policymakers, practitioners, and stakeholders to overcome the existing challenges and harness its full potential. Future research in this field should aim to broaden the scope of investigation, encompassing diverse perspectives and technological intersections, to build a more holistic understanding of AI's role in agriculture.

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Effects of Music Therapy for Psychological, Neurodevelopmental, and Neurodegenerative Disorders By Yeseo Shim[1]

Abstract

Although pharmaceutical and psychotherapy approaches are widely recognized as front-line treatment approaches for a wide range of psychological, neurodevelopmental, and neurodegenerative disorders, their effectiveness is frequently lacking. In this review, we investigate the feasibility of and evidence for music therapy in treating various physical and mental health conditions, including anxiety, depression, attention-deficit hyperactivity disorder (ADHD), and Alzheimer's diseases. Drawing on neuroscientific research, music therapy appears to be a unique treatment method that engages neural networks responsible for processing emotions and improving cognitive functions. We explore the mechanisms through which music therapy treats said disorders and delve into how music therapy affects neuroplastic changes which have long-term therapeutic effects in the brain. Finally, we highlight challenges in the existing music therapy treatment protocols and suggest ways to improve upon them.

Keywords: music therapy, anxiety, depression, ADHD, Alzheimer's disease

Effects of Music Therapy for Psychological, Neurodevelopmental, and Neurodegenerative Disorders

Although consistent efforts are being made to create and evaluate psychotherapeutic protocols, it has become clear over the years that some individuals with such debilitating conditions do not benefit from talk or pharmacological therapy. Even those who show improvements in symptoms in traditional psychotherapy might experience the desired effects too slowly that they continue to experience prolonged dysfunctioning in many aspects of their lives. Such lack of and delay in response to the available treatments call for innovative treatment modalities that can either replace or supplement existing methods. Music therapy, the use of music to address the multifaceted needs of individuals, has increasingly gathered empirical support for treating a wide range of psychological, neurodevelopmental, and neurodegenerative disorders (Raglio & Oasi, 2015). Music therapy can be applied in a clinical and evidence-based manner to help the patients achieve their specific and tailored goals and involves active engagement from both the client and therapist. Numerous types of music therapy for a wide range of physical and mental health conditions have been proposed and evaluated in the literature, with the shared goal of improving the patients' well-being using musical and therapeutic techniques. In the current article, we summarize and evaluate the empirical evidence for music therapy in treating psychological, neurodevelopmental, and neurodegenerative disorders, namely anxiety and mood disorders, attention-deficit/hyperactivity disorder, and Alzheimer's disease. Drawing from both clinical and basic science research evaluating the effectiveness of music therapy in randomized controlled trials, we suggest that music therapy provides an alternative treatment for people with a variety of neuropsychological conditions.

We first define each of the conditions discussed and their associated symptoms. Second, we review rationale for using music therapy to treat said conditions, exploring mechanisms by which therapeutic elements of music can target factors maintaining the disorders. Third, we take a closer look at the neurological evidence to gain a better understanding of the brain-mind connection by identifying the brain regions influenced by music therapy and their hypothesized effects of health outcomes. Finally, we offer our evaluations of the existing evidence for music therapy to treat each of the conditions. We make the case that music therapy is an exciting area of research with potential to enhance and supplement the existing treatment methods for psychological, neurodevelopmental, and neurodegenerative disorders.

Music Therapy for Anxiety Disorders

Anxiety is an emotional state characterized by tension, worry, fear, and physical changes, such as rapid heartbeat, shortness of breath, nausea, and vomiting that may occur as a reaction to stress and worries about future or current events (American Psychiatric Association [APA], 2013). While excessive fear or worry can lead to anxiety disorder, anxiety is a typical stress reaction. Anxiety disorders were assessed to be 7.3% prevalent worldwide (Baxter et al., 2013) and listed as the sixth most common cause of disability (Baxter et al., 2014). Moreover, anxiety disorders have been shown to cause poor quality of life (Mendlowicz & Stein, 2000), high financial and social burden (Hoffman et al., 2008), unemployment (Waghorn et al., 2005), and suicidal ideation (Boden et al., 2007). Research has indicated that even among those whose symptom severity does not meet the diagnostic threshold, many experience subclinical symptoms of anxiety at some point during their lives (Haller et al., 2014).

A meta-analysis examining 32 randomized controlled trials of music therapy for anxiety noted a significant reduction in anxiety symptoms among those who received the treatment (Lu et al., 2021). The same study found that reductions in anxiety symptoms happened across a wide range of age groups as well as countries of origin, both in developed and developing nations. Music therapy for anxiety also appears to significantly reduce symptoms of anxiety regardless of the number of sessions attended, indicating its robust effect even among those who might be less likely to complete the treatment protocol. According to the meta-analysis's findings, MT was effective in reducing anxiety compared to the control group. One explanation for such beneficial effects of music therapy for anxiety is that music can serve as a distractor, diverting a patient's focus from negative stimuli and onto something pleasant (Blood & Zatorre, 2001).

The growing understanding of neurological systems involved in music's emotional effects from healthy populations provides convincing insight to inform music therapy practice. With the exception of Fachner et al. (2013), who employed EEG to evaluate alterations in brain activity of 79 depressed participants undergoing psychodynamic improvisational music therapy, neuroimaging research involving clinical populations remains understudied. The researchers found that after three months of music therapy, patients experienced long-lasting neuronal changes in frontal midline theta. These changes were observed to correlate with improvements in

depression and anxiety symptoms as well as alpha and theta frequencies in the left fronto-temporal brain regions (Gold et al., 2013).

The effectiveness of music therapy as a treatment for anxiety in a wide range of populations could be established in the meta-analytic study by Lu et al. (2021). The results are especially reliable considering that the meta-analysis included a large, diverse sample size. However, there are notable limitations to music therapy of anxiety. The treatment has not largely been tested in non-English speaking populations. Such issues in globally implementing the treatment are confounded by the fact that there is no firmly established treatment protocol for administering music therapy for anxiety. Although the preliminary evidence supports the use of music therapy in treating anxiety disorders and reducing other comorbid psychiatric symptoms, more collaborative research is undoubtedly required to confirm the effectiveness of the treatment and harness its active therapeutic ingredients. It might be worth investigating ways to supplement existing evidence-based treatments for anxiety, such as cognitive behavioral therapy for anxiety, with the elements of music therapy. Given its cost effectiveness and ease of adoption, health systems could consider integrating music therapy into their practice to target widespread anxiety symptoms.

Music Therapy for Depression

Major depressive disorder is a widely prevalent mental health condition estimated to affect over 300 million people world wide. As a leading cause of disability and suicides, major depression is characterized by persistently depressed mood and diminished interest in pleasurable activities. People with major depression also report disturbances in sleep and appetite, low energy level, difficulty concentrating, and inappropriate guilt. While the exact etiology of depression remains unclear, it is thought to involve a wide range of genetic, biological, and environmental factors (Palazidou, 2012). Because mood disorders like major depression are often comorbid with other mental health conditions, they can significantly affect the patients' physical health and interpersonal relationships (Richards & O'Hara, 2014). Furthermore, because the symptoms of depression can be debilitating even when their severity does not cross the diagnostic threshold, it is critical to recognize and address the early signs of the disorder before they lead to serious functional impairment (Fils et al., 2010).

Music is a potent tool for influencing and regulating emotions and moods, and its therapeutic use can enhance emotional well-being (Juslin et al., 2010). While numerous kinds of music therapy protocols for depression are described in the literature, they can be categorized into two major types: active and receptive. In active music therapy, patients actively engage in spontaneous music-making with a therapist or peers through improvisation, recreation of pre-composed music, or compositional processes. The patient's active engagement in music therapy is understood to promote personal expression, insight, problem-solving, and emotional release (Bruscia, 2015). Music relationships formed during active music therapy have shown to be associated with an increased sense of self-worth and belonging as well as reduction in stress. In receptive music therapy, the patient primarily is a recipient of musical experiences in various

formats, some live and other recorded. As the recipient, patients can expect to experience shifts in consciousness, emotions, physical and mental states, and introspection. Receptive music therapy can be simultaneously administered with other therapeutic activities, such as meditation and creative expression (Bruscia, 2014). Both types of music therapy for depression are designed to provide unique opportunities for patients to experience mental well-being.

While music therapy has been piloted and tested for a wide variety of physical and mental health conditions, the exact neurological mechanisms for its beneficial effects remain unclear. Nonetheless, music therapy undoubtedly stimulates and influences human neural networks, and numerous studies have reported long-term gains in the patients (Aalbers et al., 2017). Notably, Fachner et al. (2013) observed the modulation of fronto-temporal activity in depressed patients undergoing music therapy. Specifically, the researchers noted changes in the left inferior frontal and left anterior temporal cortex. In the same study, the patients who received music therapy demonstrated improvements in processing musical and emotional information. Previous studies examining the impact of music therapy in neuronal drew similar conclusions about the pre-motor speech process activation at a laryngeal level (Koelsch et al., 2004) and neuroplastic changes in the motor cortex in the right anterior hemisphere (Schlaug et al., 2009). Together, these findings suggest that music therapy can induce neural activities in the areas of the brain responsible for emotional processing and thus lead to reductions in depressive symptoms.

A significant amount of research evidence points toward the effectiveness of music therapy in improving depressive symptoms in various populations. Alongside the primary symptom outcome measures, previous studies have noted improvements in quality of life and interpersonal functioning among patients who received music therapy for depression (Aalbers et al., 2017). In addition to reductions in distressing symptoms and improvements in quality of life, music therapy for depression also has the advantages of cost-effectiveness and patient satisfaction with treatment compared to more traditional therapeutic methods. Still, more research is needed to establish music therapy for depression as an evidence-based treatment. Without understanding how the treatment works to improve depressive symptoms, active ingredients of the treatment will remain elusive and difficult to harness for future implementations. The wide range of musical and therapeutic elements studied in the literature further complicate the standardization of music therapy for depression. To maximize the benefits of music therapy for depression, it will be critical to conduct randomized controlled trials with robust sample sizes and standardized therapeutic methods.

Music Therapy for Attention-Deficit/Hyperactivity Disorder

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental condition primarily characterized by symptoms of inattention, impulsivity, and hyperactivity. It is estimated that between 3% and 6% of the children worldwide have ADHD, with boys being 3 times more likely to be diagnosed than girls. Although the symptoms of ADHD often first appear in childhood, they can appear and persist throughout time (Barkley, 1998; Tannock, 1998). Irritability, difficulty in delaying responses, blurting out answers before questions have been

completed, difficulty awaiting one's turn, and frequently interrupting or intruding on others to the point of causing difficulties in social, academic, or occupational settings are all instances of impulsivity, according to the DSM-IV criteria (APA, 2013). Furthermore, between 50% and 80% of children diagnosed with ADHD also meet the criteria for other psychological disorders, most commonly anxiety, mood, and developmental learning difficulties, as well as other disruptive behavior problems.

Interestingly, music therapists and researchers have observed that children and adolescents with ADHD exhibit disordered beating, or difficulty maintaining a consistent beat or rhythms, often due to poor impulse control (Barratt, 1983). The capacity to pay attention to incoming stimuli, estimate time durations, and effectively plan and execute a response are some of the characteristics that determine one's ability to reproduce motor timing tasks accurately. Previous studies have indicated that individuals with ADHD have impaired timing, and timing impairment is associated with impulsive behaviors, indicating the association between working memory and inhibitory control (Smith et al., 2002). Moreover, distraction, both internal and external, can negatively impact working memory and disrupt motor responses.

Various music therapy techniques have supported effectiveness with adolescents (Aigen, 1997). Creating organized music, in groups and peers, requires a significant amount of attention and self-control. Moreover, practicing and rehearsal of rhythmic tasks have shown to enhance internal organization and impulse control (Thaut, 1992). A consistent beat required to participate in active music therapy for ADHD can help and hold clients' attention as well as improve body awareness and motor coordination (Bunt et al., 2013). To manage the difficulties of maintaining intricate rhythms in music therapy for ADHD, Rickson and Watkins (2003) hypothesized that children with ADHD could get overstimulated in artistic music-making settings. Instead of complex and variable rhythmic patterns often seen in music therapy, the researchers programmed highly structured and predictable rhythmic activities and confirmed that children with ADHD are more likely to benefit from structured, predictable programs.

There are several aspects of music that could be therapeutic for children with ADHD at the neuronal level. These include brain activation in both hemispheres (Hannaford, 1995), the ability of music to improve learning and memory (Wolfe & Horn, 1993) and the effect of particular sounds or tones on brain wave production. All forms of musical expression, such as instrumental improvisation, musical play, and group singing require some form of physical movement, therefore engaging in a wide area of neural networks in both hemispheres. Music and movement can heighten emotional and spatial awareness, while musical play and group singing are likely to pair music with auditory perception and memory. Music therapy has also shown to improve the effects of dichotic listening which leads to increase in short-term memory and information processing and decrease in distractibility (Morton et al., 1990). All methods utilize sound and tones, which may modulate brainwave activity. However, more research is required to fully understand how music can be effectively applied in treating children with ADHD.

As is the case with music therapy for other types of neurological and psychological conditions, the biggest limitation of music therapy for ADHD is the lack of standardized

treatment protocols. It is also especially difficult to evaluate the empirical evidence in adolescent populations because symptom changes in children could be due to their expected development over time. Still, there appears to be some evidence to suggest that high levels of structure in music therapy is beneficial for children and adolescents with ADHD. It is also worth considering that adolescents with ADHD could benefit from group improvisational music therapy due to participant motivation and the instant benefits of creating music together. Though definitive conclusions cannot be made about active ingredients of music therapy for ADHD, the current literature on the topic indicates that overall, music therapy can help reduce a variety of ADHD symptoms both in the classroom and home settings. Targeting these symptoms at such a critical neurodevelopmental stage will undoubtedly be important in alleviating problems caused by impulsivity and other symptoms of ADHD in the children's development trajectory.

Music Therapy for Alzheimer's Disease

Alzheimer's disease is a neurological disorder estimated to occur in 5% of people over the age of 65 worldwide, with the prevalence exponentially increasing with age (Ferri et al., 2005). As the leading cause of dementia, Alzheimer's disease affects people both neuropsychologically and cognitively. People with Alzheimer's disease experience increased depressed mood and apathy in addition to the hallmark symptoms of cognitive loss and executive functioning difficulties (Geda et al., 2013). Although numerous pharmacological treatments have been proposed and tested to manage said symptoms, none of them have demonstrated long-term clinical efficacy. Thus, without the existence of a singular cure that treats both neuropsychological and cognitive symptoms of dementia, complementary treatment options have gained increasing attention for managing Alzheimer's disease (Särkämö et al., 2014). Among them, music therapy for Alzheimer's disease has shown promising results in improving patients' mood and cognitive functioning. In fact, cognitive training and music therapy have accrued decades of evidence demonstrating improvement in symptoms of dementia (Lorusso et al., 2018).

No separate music therapy protocol, to our best knowledge, has been proposed and empirically evaluated for treating Alzheimer's disease and other neurological disorders related to cognitive impairment. Nonetheless, music interventions have shown to improve mood, cognitive and executive functioning, and memory in a wide range of populations (Koelsch, 2014). Specifically, among older populations, studies have suggested that musical training can slow down age-related cognitive and memory impairments. Patients with Alzheimer's disease who received music therapy demonstrated improved categorical world fluency and autobiographical memory (Thompson et al., 2015). Furthermore, music therapy provides opportunities for patients and caregivers to explore ways to express their thoughts and feelings beyond verbal communications that might have been negatively impacted by the symptoms of Alzheimer's disease. Such increases in positive interactions between patients and caregivers have been associated with positive health outcomes (Dyer et al., 2018).

In healthy populations, it has been well documented that music can induce neuroplasticity and sensations of welfare and pleasure by stimulating subcortical circuits, the limbic system, and the emotional reward system (Soria-Urios et al., 2011). Similarly, both the developing brain of children and the adult brain have shown to benefit from long-term training in music and associated skills (Schlaug, 2015). Alzheimer's disease has shown to damage neural networks in the brain and result in a wide variety of cognitive deficits. Interestingly, previous studies have demonstrated that music can stimulate reminiang healthy neural networks (Platel et al., 2003; Jacobson et al., 2015). Specifically, functional magnetic resonance imaging of the patients' brains revealed that music can activate the brain regions critical for encoding long-term memory, the caudal anterior cingulate and the ventral pre-supplementary motor area. These two brain regions were shown to be less negatively affected by Alzheimer's disease than the other parts of the brain also involved in encoding long-term memory. Together, these findings hint that music therapy may be especially effective for patients with Alzheimer's disease because they are still able to retrieve verbal and musical memories.

To many, playing and listening to music is simply a pleasant activity conducive to positive emotions and social interactions. Music can also be personalized to each patient's preference to enhance the beneficial effects. Personal anecdotes and research evidence indicate that music alleviates stress (Gómez & Gómez, 2017) and promotes mental health by releasing several neurotransmitters, such as endorphins and dopamine (Chanda & Levitin, 2013). Music therapy for Alzheimer's disease and symptoms of dementia, however, has not gathered conclusive evidence supporting its efficacy. The lack of such conclusive evidence is driven by the design of the trials that have been conducted so far. For many of them, their sample sizes are too small to detect significant differences between study groups. Perhaps more importantly, music interventions vary widely, and so do the methods to measure cognitive functioning and other areas of life affected by Alzheimer's disease (Chanda & Levitin, 2013). Music therapy as a standalone treatment for Alzheimer's disease will most likely remain unfeasible as the condition significantly affects almost all aspects of the patient's functioning.

Evidence for music therapy in the literature has been mixed. Although numerous studies have demonstrated its positive effects in improving cognitive functioning and mood among the patients' with Alzheimer's disease, the lack of standardization in the treatment protocol makes it extremely challenging for researchers to draw a strong conclusion about its efficacy (Moreno-Morales et al., 2020). Still, music is a noninvasive intervention with no known side effects and costs far less than the alternative pharmacological treatments (Gómez & Gómez, 2017). Given such upsides of music therapy, more robust randomized controlled trials with standardized clinical techniques are warranted. These trials will not only provide a greater empirical basis for the treatment but also have the potential to identify crucial mechanisms in treating the disease that can be leveraged in other treatments. While it remains unclear how to best incorporate music therapy in the treatment and management of Alzheimer's disease and symptoms of dementia, music therapy continues to be growing in its research evidence and will require continued support from the scientific community.

Summary and Conclusion

In conclusion, the paper suggests that there is much to be learned from music-therapy and highlights the potential of music therapy across psychological, neurodevelopmental, and neurodegenerative disorders. This review established a foundation for a more sophisticated understanding of how music therapy might function as a competitive alternative to conventional therapeutic interventions by fusing cross-disciplinary research and empirical data. The paper leads to further inquiry and development into the establishment of standardized treatment, the therapy's long-term effects, and the brain mechanisms underlying the therapy. By addressing these problems, we may strengthen and improve the empirical foundations of music therapy, increase its application, and develop more effective and practical treatments for a range of conditions worldwide.

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The Making of "Cure", an Adventure-Based Story Game By Qi Feng

Abstract

This paper analyzes the steps taken to develop my game, Cure, which is made on Unreal Engine 5. "Cure" is a story-based game following the life of an adopted fox trying to save his master from an "incurable" disease. Unreal Engine is a game development and 3D animation software similar to Unity, but it uses blueprints instead of code morsels. The game will be made public in the near future, as it's still in the developmental stage for now.

Introduction

This post-mortem analysis delves into the development process of Cure, a 3-dimensional adventure game, and explores the triumphs and setbacks faced during its creation.

Premise

The inception of "Cure" in the summer of 2023 marked the beginning of a creative voyage to bring a compelling narrative to the interactive world of gaming. The conceptual seed was planted by a short story that captivated my imagination—a tale of loyalty, mysticism, and the indomitable spirit of an animal companion. In designing the game's framework, I drew a wealth of inspiration from genre-defining titles such as "Breath of the Wild" and "Tears of the Kingdom." These games set a benchmark for open-world exploration, with their vast landscapes, intricate puzzles, and profound sense of adventure. "Cure" was envisioned to be a tapestry woven with similar threads, creating an experience that would immerse players in an adventure that was both familiar in its homage to its inspirations and unique in its own narrative and gameplay.

With Unreal Engine as the foundation, the development of "Cure" aimed to harness the engine's superior capabilities to craft an adventure-filled world—a place where every hill, valley, and ancient ruin held the promise of discovery. The protagonist of this world is Theo, an anthropomorphic fox with a heart as vast as the open world he traverses. Theo's journey is driven by a series of challenges, embodied by puzzles that require both wit and agility and cutscenes, or story panels, that enrich the storyline. Players guide Theo through diverse terrains (see Figure 1), each meticulously designed to provide not only visual splendor but also a playground for the mind's puzzle-solving faculties. The gameplay intertwines traditional control mechanisms with intuitive puzzle elements, ensuring that the act of guiding Theo is both engaging and rewarding.

At the heart of "Cure" is a narrative steeped in emotional depth. Theo's quest to collect magical rune stones is more than a mere collection endeavor; it is a race against time to save his ailing owner, instilling a sense of urgency and purpose in the gameplay. This narrative drive is complemented by the game's cutscenes, which are crafted to not only advance the story but also to provide windows into Theo's soul, his memories, and the bond he shares with his owner. The cutscenes are cinematic interludes that offer players respite from the gameplay while simultaneously deepening their connection to the world and its characters. The use of Unreal

Engine facilitates a seamless blend of gameplay and storytelling, with each element enhancing the other to create a cohesive and compelling player experience.

The development is not just an endeavor to create another game; it is an aspiration to offer an odyssey that resonates with players on a personal level, inviting them to become a part of Theo's world and story. The game seeks to leave an indelible mark on the hearts of its players, much like the stories that inspired its creation.
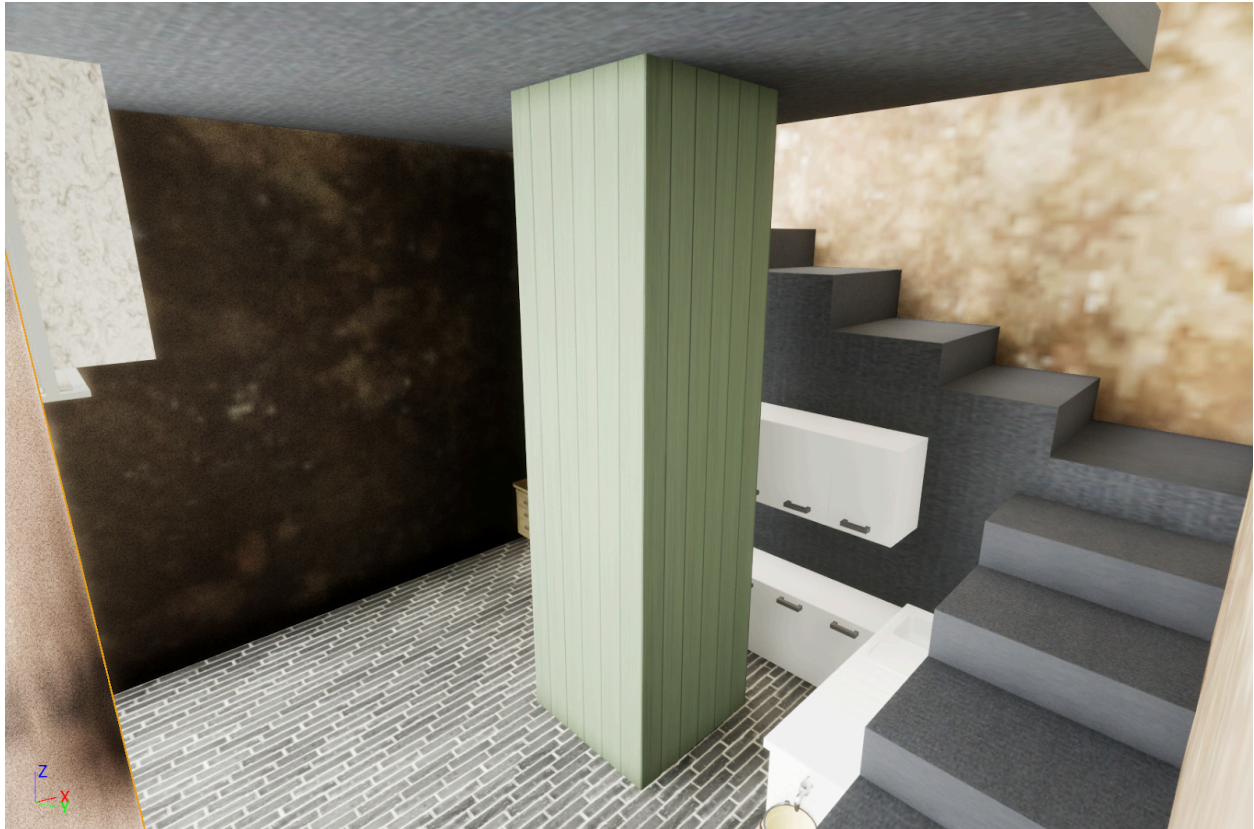
Figure 1: Screenshot of one of *Cure*'s environments.
Unreal Engines vs Other Technical Tools

Why Unreal Engine?

The choice of a game engine is a pivotal decision in the development of a video game, which can have far-reaching implications on the game's design, functionality, and success. Among the myriad options available, Unreal Engine emerges as a leader for a host of reasons. In this comprehensive examination, we contrast Unreal Engine's features with those of other popular game development tools: Unity, and programming languages such as Java, Python, C++, and C#.

Unreal Engine and Traditional Programming Languages:

When comparing Unreal Engine to traditional programming languages like Java, Python, C++, and C#, it is important to note that Unreal Engine itself is built upon C++. This gives it the

performance edge inherent to compiled languages, crucial for real-time applications like games. Java and Python, while powerful and versatile in their own right, are generally not as performant as C++ for game development due to their nature as interpreted languages. Java is often associated with cross-platform applications and server-side solutions, whereas Python excels in areas like artificial intelligence, data analysis, and scripting for small-to-medium-sized tools.

Unreal Engine vs. Unity–Graphics and Performance:

Unreal Engine is renowned for its advanced graphics and high performance, often seen as the standard for AAA titles that require cutting-edge visual fidelity. It uses physically-based rendering, dynamic lighting, and a powerful particle system that can produce cinematic-quality visuals right out of the box. Unity, while capable of beautiful visuals, often requires additional tools and assets to reach similar levels of graphical prowess. In terms of performance, Unreal Engine's native use of C++ allows developers to extract more from the hardware, optimizing for speed and efficiency, which is crucial for games with extensive graphical demands and complex simulations.

When comparing the system requirements for Unreal Engine and Unity, it is essential to recognize that these requirements can vary based on the complexity of the project you are developing. However, we can discuss the general requirements needed to run each engine effectively for most development tasks.

Unreal Engine System Requirements

Unreal Engine is known for its high-fidelity graphics and powerful rendering capabilities, which naturally demand more robust system specifications. The minimum requirements to run Unreal Engine typically include a 64-bit processor, a quad-core Intel or AMD processor, 8 GB of RAM, and a DirectX 11 or DirectX 12 compatible graphics card. However, these minimum requirements are often insufficient for practical development, especially when working on more graphically intense projects. Developers would benefit from a faster multi-core processor, 16 GB or more RAM, and a dedicated graphics card with significant VRAM (e.g., NVIDIA GTX 1060 or higher). For developers aiming to work with VR, higher-end graphics cards such as an NVIDIA RTX series are recommended ("Unreal Hardware and Software Specifications").

Storage is another consideration; an SSD is highly recommended for faster load times and overall performance improvement when working with Unreal Engine. Furthermore, depending on the project's size, developers may require a significant amount of storage space, often starting at 256 GB and increasing ("Unreal Hardware and Software Specifications").

Unity System Requirements

Unity is designed to be more accessible, with system requirements that are generally lower than those of Unreal Engine. The minimum requirements for running Unity include a 64-bit processor, a dual-core CPU, 4 GB of RAM, and a graphics card with DX10 (shader model 4.0) capabilities. These specs can handle small to medium-sized projects comfortably. However,

for more demanding projects, particularly those that utilize Unity's High Definition Render Pipeline (HDRP) for better visuals, the requirements increase. A developer would be better equipped with a multi-core processor, 8 GB or more of RAM, and a graphics card with DX11 or DX12 support and ample VRAM ("System requirements for Unity").

Like Unreal Engine, using an SSD over a traditional hard drive can significantly impact Unity's performance, making it a recommended choice. The amount of storage needed can vary, but developers should have at least 30 GB of free space available, with more required for larger projects ("System requirements for Unity").

Both Unreal Engine and Unity have scalable system requirements, but Unreal Engine typically requires a higher-end setup to utilize its full capabilities, especially for rendering complex scenes and leveraging its advanced features. Unity can run on less powerful hardware, but for larger projects or those requiring high-end graphics, the requirements become similar to Unreal Engine.

The choice between Unreal Engine and Unity might also be influenced by the target platform for the game being developed. If the end product is intended for platforms with lower specifications, Unity might provide a smoother development experience. Conversely, for high-end PC games or console games that push the limits of current hardware, Unreal Engine could be the more suitable choice.

Developers must balance the system requirements with their project needs, budget, and hardware availability. Both engines offer free versions that developers can download and test on their systems to gauge performance before committing to a project. This hands-on experience is often the best way to determine whether the system requirements will suffice for the intended development work.

Development Workflow:

In terms of development workflow, Unreal Engine offers the Blueprint visual scripting system, a feature that allows developers to create game logic without writing traditional code (See Figure 2), which can significantly speed up development and lower the barrier to entry for non-programmers. Unity, while it has introduced its own visual scripting tools, historically relies more on traditional coding in C#, which can be more accessible for developers with a background in object-oriented programming. Unity's environment is generally considered more user-friendly, and its asset store provides a wealth of resources that can further accelerate development, which can be particularly appealing for smaller studios or independent developers.
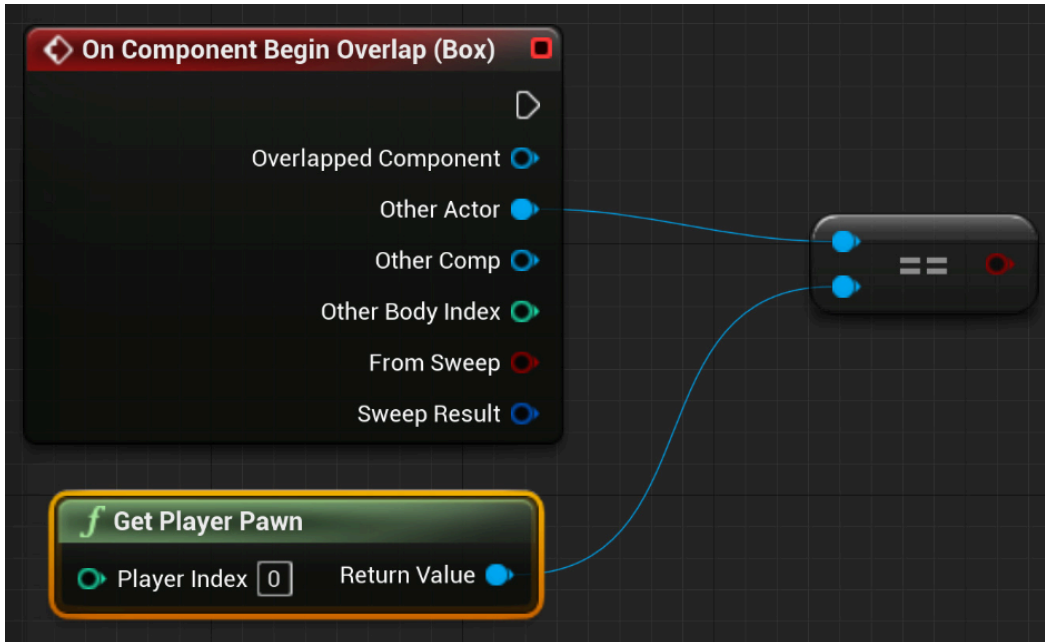
Figure 2: Screenshot of Unreal's Blueprints. Taken from "Blueprints Visual Scripting".

Community and Ecosystem:

Both Unreal Engine and Unity boast strong communities and ecosystems. Unreal Engine's community is especially active in professional and high-end game development circles, with extensive documentation and a marketplace filled with high-quality assets. Unity's community is broader, encompassing a wide range of developers from hobbyists to professionals, and benefits from a large asset store and a vast array of tutorials and forums. Unity's long-standing presence in the industry has cultivated a rich ecosystem of third-party tools and extensions that can enhance the engine's capabilities.

Unreal Engine vs. Java–Performance and Use Cases:

Java is a versatile language with a strong presence in enterprise applications, web services, and mobile development, but it is less prevalent in high-end game development. The primary reason is performance; Java is an interpreted language running on a virtual machine, which adds overhead that can be prohibitive for the computational demands of modern games. In contrast, Unreal Engine's foundation in C++ allows for direct hardware interaction, providing the necessary performance for real-time rendering and complex physics calculations that Java typically cannot match.

Cross-platform Development:

Java's write-once-run-anywhere philosophy has made it a favorite for cross-platform application development. However, this advantage is less significant in game development, as both Unreal Engine and Unity offer robust cross-platform support. Unreal Engine, with its advanced rendering capabilities, can deploy to multiple platforms without sacrificing

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high-quality visuals, whereas Java-based games might struggle to maintain consistent performance across different devices.

Development Environment:

Java offers a mature development environment with tools like Eclipse and IntelliJ IDEA, which have extensive features for code analysis, refactoring, and testing. Despite these strengths, Java lacks the specialized tools for game development that Unreal Engine provides. Unreal Engine comes with a full-fledged editor designed specifically for building games, including level design, animation, lighting, and material editors, all integrated into one environment, making it a more suitable choice for game developers.

Unreal Engine vs. Python–Ease of Use vs. Performance:

Python is celebrated for its simplicity and readability, making it an excellent choice for beginners and for rapid application development. It is widely used in scripting, data analysis, machine learning, and web development. However, Python's ease of use comes at the cost of performance, as it is an interpreted language with significant overhead compared to compiled languages. Unreal Engine's use of C++ ensures that games run with maximum efficiency, which is essential for the resource-intensive nature of modern gaming.

Tooling and Libraries:

While Python has a vast array of libraries for various applications, it lacks the specialized game development tools that come with Unreal Engine. Unreal provides a complete suite of tools tailored for game development, including a powerful editor, advanced animation systems, and a physics engine, which are not naturally part of Python's ecosystem. Python can be used in game development as a scripting language within engines or for creating simple games with libraries like Pygame, but it doesn't offer the same level of control and optimization for serious game development.

Integration with Other Technologies:

Python's interoperability with other technologies is one of its strong suits, often serving as a glue language that integrates different systems and workflows. However, in the context of game development, Unreal Engine's integration capabilities are more relevant. Unreal Engine can seamlessly integrate with industry-standard software like Maya or Photoshop, and it also allows for the incorporation of C++ libraries directly into the game project, which can be critical for performance and functionality in games.

Unreal Engine vs. C++ and C#--Language Foundations:

Unreal Engine is built on C++, giving it access to low-level system resources and high performance, which is essential for developing complex games with extensive graphical and computational requirements. C++ provides the control needed to optimize every aspect of a

game, from memory management to multi-threading. While C# is used in Unity and is easier to learn and use, it does not offer the same level of performance and control as C++, primarily due to its garbage collection and higher abstraction level ("Best Unreal Engine 5 Language").

Development Speed and Productivity:

C# offers rapid development and a gentler learning curve, which can lead to quicker prototyping and productivity, especially for smaller projects or those with less stringent performance requirements. However, Unreal Engine's Blueprint system ("Blueprints Visual Scripting") can bridge this gap, allowing developers to create prototypes and gameplay elements without deep knowledge of C++ syntax. This makes Unreal Engine competitive in terms of development speed while retaining the performance advantages of C++.

Ecosystem and Support:

Both C++ and C# have extensive ecosystems and support communities. C++ has been a staple in software development for decades, offering a wealth of libraries, compilers, and tools. C#, primarily through Unity's ecosystem, has a vast array of assets, plugins, and a supportive community that can be invaluable for game development. Unreal Engine benefits from the robustness of the C++ ecosystem while also providing a comprehensive platform with a strong community, extensive documentation, and a marketplace, making it a comprehensive choice for game development.

The decision to use Unreal Engine over Unity, Java, Python, C++, or C# hinges on several factors: the need for cutting-edge graphics, robust physics simulations, and a comprehensive suite of development tools. While each of the other options has its strengths and ideal use cases, Unreal Engine offers a combination of power, flexibility, and industry-standard capabilities that make it an unparalleled choice for game development projects aiming for the highest quality and performance.

Game–What Went Well:

Cure seamlessly blends cutscenes, exploration, tutorials, and minigames, offering players a holistic gaming experience. We use standard keyboard-based motion controls (mouse for camera, WASD to move). Movement, guided by W, A, S, and D keys, propels players through a world of intricate puzzles. An ingenious addition to the game is the "scent trail," a transparent guide leading players to pivotal story points. The game's modern setting ensures a relatable experience, even as players traverse different countries, with meticulous attention to details such as music, speech, and everyday objects.

There are a number of resources and design decisions that contribute to the successful parts of the project. Utilizing Unreal Engine and Blender, while initially daunting, has opened avenues for creativity. YouTube tutorials provide a foundational understanding, fostering independence in game development. The diverse demographic appeal of Cure, suitable for all

maturity levels, coupled with straightforward controls, enhances its accessibility and broadens its potential audience.

There are some tips and tricks used to solve/bypass problems. First of all, debugging is an essential must-know. Using Unreal's On-screen print statements to see which parts are running correctly is an incredibly effective way of quickly pinpointing errors. Furthermore, using reference documentation to make sure the correct blueprints are used is essential to differentiate commands with duplicate names.

On-screen Print Statements in Unreal Engine

A critical aspect of game development in Unreal Engine is the ability to debug effectively, and one of the most reliable tools for this is the use of on-screen print statements. These statements serve as a real-time debugging aid, outputting valuable information directly onto the screen, which allows developers to track the execution of code and pinpoint the location of bugs. This feature is particularly useful when testing new game mechanics or when trying to understand the flow of complex blueprint scripts. By strategically placing print statements throughout the blueprint nodes, we can visualize variable values, execution order, and the state of the game at any given moment. This immediate feedback loop is crucial for rapid iteration and troubleshooting, ensuring that developers can maintain a swift and efficient workflow.

When it comes to managing a large number of blueprints, especially those with duplicate names or similar functionalities, reference documentation becomes indispensable. It is imperative to ensure that the correct blueprints are being referenced and modified, as a single oversight can lead to hours of debugging and confusion. This is why maintaining a well-organized and thorough reference document is essential. Such documentation acts as a map, guiding the developer through the intricacies of the game's architecture and helping to avoid the pitfalls associated with managing numerous blueprints. By keeping an up-to-date reference, developers can quickly locate the necessary blueprints, understand their interconnections, and ensure that any adjustments are made in the correct context.

Niagara System and Homing Objects

The Niagara System in Unreal Engine is a potent and versatile tool for creating and controlling particle effects. It allows developers to craft detailed and dynamic visual effects that are integral to the immersive experience of a game. A specific use case where the Niagara System shines is in the creation of homing objects. These are objects or particles programmed to "home in" on a target, which can be a character, an item, or a location in the game world. To ensure that these homing mechanisms work as intended, it is crucial that the target is neither too close nor too far from the particle. If the target is too distant, the homing object may not initiate its pursuit, or it might take an impractically long time to reach its destination, both of which can detract from the gameplay experience. Conversely, if the target is too close, the homing effect might not be noticeable or visually impressive. Therefore, careful calibration of the distance between the homing object and its target is vital to achieving the desired effect in the game.

The implementation of the Niagara System's homing capability demands a nuanced understanding of both the system's parameters and the game environment. It involves not only setting the right distance but also fine-tuning other factors such as speed, acceleration, and the behavior of the object upon reaching its target. These elements must be balanced to produce a natural and satisfying outcome that supports the game's design. Moreover, the use of homing objects often requires rigorous testing and iteration to perfect their behavior within the game's context. By mastering the Niagara System's parameters and carefully considering the gameplay mechanics, developers can create engaging and visually appealing effects that enhance the player's experience.

One of the key successes in the development of "Cure" was the seamless introduction of subjects and narrative elements to the player. This was achieved through the adept utilization of Unreal Engine's media and media widget blueprints. Typically, subject introductions in games serve the dual purpose of driving the narrative and acquainting players with new characters, mechanics, or important plot points. In "Cure," we endeavored to make these introductions not just informative but also engaging.

To accomplish this, we construct a series of media blueprints that allow us to embed video content directly into the game environment. This approach means that players could witness the story unfold through a dynamic and cinematic lens, providing context and background in a format that was both accessible and visually appealing. Especially in a video format, the ability to present subject matter through media blueprints is invaluable, as it combines auditory and visual learning to reinforce player engagement.

Adapting to Cutscene Tool Limitations

My vision for "Cure" is cinematic at its core, intending to weave gameplay and narrative into an inseparable tapestry. Unreal Engine 5's built-in sequencer came with the promise of creating cinematic experiences with ease, but as the narrative ambitions of "Cure" grow, we find the sequencer's capabilities to be limiting for our specific creative needs. The sequencer, while robust in many ways, sometimes lacks the nuanced control over timing and the depth of editing features required for the intricate, multi-layered cutscenes we had storyboarded. The narrative I wish to tell through "Cure" is not just a sequence of events but a complex interplay of emotions, character development, and pivotal plot points that require a cinematic treatment akin to that of a feature film. In pursuit of this cinematic finesse, we explore external tools and land on Adobe Premiere Pro, a decision that marks a significant turning point in the production of our cutscenes.

Adobe Premiere Pro, a stalwart in the video editing industry, offers a plethora of editing tools that grant us the freedom to manipulate our footage with a granular level of precision. Here, we could slice frames with surgical accuracy, control the pacing to match the emotive beats of the story, and composite layers upon layers to craft scenes that were as rich visually as they were rich narratively. This external environment also allows for the integration of various visual effects and audio tracks that enrich the cinematic quality of each scene. The flexibility of Premiere Pro enables us to experiment with a comic-book style, a creative choice that aligns well

with the game's aesthetic. This style, characterized by bold colors, dynamic transitions, and stylized frames, allows us to present our cutscenes in a way that pays homage to the graphic novels that have inspired portions of our narrative. The process is meticulous; each scene is crafted with an artist's touch, frame by frame, ensuring that every second of the cutscene conveys the intended emotion and narrative thrust.

Upon completion, these cutscenes are not standalone pieces but integral parts of the game's fabric that need to be woven back into the interactive experience. The challenge then becomes integrating these externally edited sequences into the Unreal Engine without disrupting the immersive flow of the game. This is achieved through careful planning and technical ingenuity, ensuring that transitions between gameplay and cutscenes are smooth and that the stylistic choices made in Adobe Premiere Pro are reflected accurately within the game engine. The result is a collection of cutscenes that not only carry the narrative forward but also do so with a distinct style that sets "Cure" apart. These sequences were polished, not merely in their visual appeal but in their ability to carry the player through the emotional journey of the game. The narrative-driven sequences thus become a hallmark of "Cure," enhancing the storytelling and providing players with a cinematic experience that complements the interactive elements of the game.

This creative solution to our cutscene conundrum is emblematic of the adaptive and innovative spirit that defined the development of "Cure." It is a testament to the team's resilience and our collective commitment to the game's artistic vision. By stepping outside the confines of the expected, we embrace a solution that enriches "Cure" and showcases the potential of integrating traditional filmmaking techniques into modern game development. The seamless melding of these cutscenes with the gameplay was a technical achievement, but more importantly, it is a narrative triumph. Each cutscene became a window into the soul of "Cure," offering players a deeper connection to the game's world and its characters. In doing so, we not only overcame a technical hurdle but also elevated the art of storytelling within the interactive medium.

Leveraging Community Insights and Support:

The collective wisdom and experience of the Unreal Engine community has played an instrumental role in the development of "Cure," offering a reservoir of knowledge and support that was critical to overcoming the technical and creative challenges we faced. In the vast digital landscape where information is both abundant and fragmented, the Epic Games Unreal Engine Community forums became a beacon, illuminating the path through complex development mazes with peer-reviewed solutions and expert advice. Here, veterans and novices alike converge, forging an invaluable resource for developers seeking guidance or validation of their approaches. The community's culture of sharing and support not only accelerates problem-solving but also fosters a sense of camaraderie among developers, which is often the much-needed morale boost during the grueling development cycle.

Moreover, the official documentation serves as our fundamental textbook, a compendium of the engine's capabilities, and a guide to its vast functionalities. While exhaustive, the official documentation could not always encapsulate the nuance of real-world application, a gap adeptly filled by the myriad of YouTube channels dedicated to Unreal Engine development. Channels such as Buvesa Game Development, BeardGames, and MattAspland transformed abstract concepts into tangible examples, demonstrating the implementation of features in actual game scenarios. These content creators, with their didactic videos, not only demystify complex topics but also offer a variety of creative techniques and workarounds that are not apparent in the official literature. Their content became a form of mentorship, providing step-by-step tutorials that have been pivotal in the successful integration of various game mechanics within "Cure."

The symbiotic relationship between content creators and game developers is a hallmark of the Unreal Engine ecosystem. By sharing their development journeys, successes, and even failures, these creators have built libraries of case studies that serve as a collective memory for the community, ensuring that hard-earned lessons are passed on and not repeated. It is within this shared digital space that "Cure" has found its technical footing, adapting the insights and lessons from these virtual mentors into its development DNA. From debugging perplexing issues to optimizing performance, every piece of advice was a puzzle piece that, when correctly placed, reveals a larger picture of game development harmony.

The community's diverse perspectives also provide a crucible for testing ideas and soliciting feedback. Whether it is a forum post dissecting the nuances of the Blueprint system or a live stream detailing the art of level design, every interaction is an opportunity to learn and grow. Peer reviews and collaborative discussions often led to a refinement of features within "Cure," ensuring that the game not only meets the expectations of its creators but also resonates with the community that had become an integral part of its development journey.

In essence, the community around Unreal Engine is not merely a support system; it is a thriving ecosystem that nurtured the growth of "Cure" from a concept to a living, breathing digital experience. It is within this ecosystem that "Cure" has evolved, guided by the collective intelligence of thousands of developers, each contributing a verse to the epic that is game development. As "Cure" prepares to make its mark on the gaming world, it stands as a testament to the power of community, the value of shared knowledge, and the strength found in unity. It is a product not just of a single vision, but of a shared passion for creating worlds that captivate, challenge, and inspire.

What Did Not Go Well:

Despite the progress, challenges emerged, notably in the realm of programming using Unreal Engine's Blueprints.   The Blueprints system, while powerful and visually intuitive, presented a steep learning curve. My initial forays into the Blueprint scripting often ended in a labyrinth of errors and bugs that seemed insurmountable. The inability to use traditional text-based code meant that I could not simply search for solutions or copy error messages into search engines or AI platforms like ChatGPT. This limitation of the visual scripting system led to

many frustrating hours, as it felt like I was trying to decipher an alien language without a translator. Each session ended with a gnawing sense of defeat, as I faced the cold reality that conventional coding strategies were of little use here.

This frustration was compounded when working with the Niagara System, Unreal Engine's advanced particle system, which proved to be one of the most challenging aspects of development. Trying to perfect the "scent trails" mechanic, a feature designed to guide players along their journey, felt like grappling with a shape-shifter—each time I thought I had a grip on the issue, a new, unexpected error would emerge. Despite poring over forum posts, watching countless tutorial videos, and experimenting with various configurations, the solution to my problems with the Niagara System remained tantalizingly out of reach. It was a humbling reminder that game development was as much about perseverance as it was about creativity.

The breakthrough came through dedicated learning and mentorship. My mentor, Sam, provided invaluable insights into the intricacies of debugging in Unreal Engine. With Sam's guidance, I learned to utilize Unreal's on-screen print statements effectively, transforming the way I approached problem-solving within the Blueprint environment. I began to dissect my Blueprints, using print statements to isolate and identify the faulty logic and incorrect variables. This methodical approach to debugging turned what once felt like a guessing game into a structured process. Sam also helped me realize the importance of referencing the correct character arrays within Blueprints, which was the key to making the homing Niagara system recognize its targets. The moment I corrected this, it was as if a fog had lifted, and the game's features began to work in harmony. This mastery over debugging not only solved my immediate issues but also equipped me with the tools and confidence to tackle future challenges head-on, turning frustration into empowerment and uncertainty into clarity.

Conclusion/Final Thoughts:

The odyssey of creating "Cure" has been more than just a technical endeavor—it has been a journey of personal and professional growth, pushing the boundaries of my capabilities as a game developer. The culmination of this project is not solely measured by the completion of the game but also by the rich tapestry of skills woven throughout the development process. From the nuanced art of storytelling to the intricate technicalities of Unreal Engine, each challenge surmounted has been a lesson in both the art of game design and the science of its execution. These experiences have not only sharpened my technical acumen but also deepened my appreciation for the narrative potential of the medium.

The development of "Cure" has also provided valuable insights into the collaborative nature of game creation. Through interactions with the community, the support of mentors, and the feedback from early testers, I have learned that the creation of a game is a symphony played by many hands. Each contribution, whether a line of code or a piece of conceptual art, is a note in the larger composition that is "Cure". This collaboration has taught me the importance of open communication, the value of diverse perspectives, and the strength found in collective problem-solving.

Looking forward, "Cure" stands as a testament to the power of interactive storytelling and the emotional resonance that games can carry. It is my hope that Theo's journey will not only entertain but also evoke a deeper empathy and connection within players. In an industry often fixated on graphical prowess and mechanical innovation, "Cure" aspires to remind us that at the core of every great game is a story that touches the heart. As I prepare to release "Cure" into the world, I do so with the anticipation that it will contribute meaningfully to the evolving dialogue of what games can be and the experiences they can offer.

As this chapter of development closes and another awaits its beginning, I carry with me the knowledge that the challenges faced were not roadblocks but stepping stones—opportunities to ascend to greater heights in game development. "Cure" is more than a game; it is a chapter in my life, a bridge to the future, and a beacon for others who dare to dream and create. With its release, I invite players and developers alike to partake in the journey of Theo and find within it a source of inspiration, reflection, and above all, a cure for the common game.

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Coral Reef Trophodynamics in Changing Seas By Navya Putrevu

Abstract

One of the most vulnerable ocean ecosystems in the world, coral reefs are threatened by a variety of complex factors, mostly anthropogenic at their base. While coral bleaching remains the most well-known threat to coral reefs, this is only one of many factors contributing to the degradation of these environments and the breakdown of the communities that inhabit them. This review aims to look at the complex trophic interactions within a coral reef ecosystem by dividing these interactions into the two primary tiers of trophic control observed: top-down and bottom-up control. A meta-analysis and summary of selected research reveal insights on shifting tier-based interactions and ecological consequences of the disruption of these trophic modes within a coral reef environment.

Introduction

The study of trophic systems has intensified over the decades as instances of collapses, cascades, and disruptions have increased. Shifting ecosystem balances have been observed in countless forms all across the world, with ecological upsets originating from all trophic levels. In coral reefs, understanding these trophic system disruptions and both their direct and indirect effects is crucial to the management of these already highly vulnerable ecosystems (Bellwood et al., 2004; Bierwagen et al., 2018).

Top-down control refers to the effects exerted by top consumers on an ecosystem (Bauman et al., 2019). Perhaps the most dramatic and well-known instance of top-down control is exemplified in trophic cascades. This ecological phenomenon became famous due to the dramatic environmental effects witnessed during Yellowstone's wolf removal and subsequent reintroduction. As true in Yellowstone as anywhere else, this mode of trophic control has the potential to not only change the species assemblage of an ecosystem but has also been observed to physically reshape an entire ecosystem (Beschta & Ripple, 2016). The effects of top-down control are usually easily and immediately visible to the naked eye. Medium-sized predators and even grazers contribute immensely to this level of trophic control (Dale et al., 2011).

Bottom-up control centers around the role of microorganisms and nutrient abundance within coral reef ecosystems (Littler et al., 2006). Despite proving difficult to observe directly, the disruptions at this level have an immeasurable impact on all other organisms. These factors are both biotic and abiotic in origin but fundamental to the health and function of an ecosystem (Littler et al., 2006; Smith et al., 2010; Garren & Azam, 2011).

Top-Down Control in Coral Reef Ecosystems

Top-down control plays a crucial role in shaping coral reef ecosystems (Bauman et al., 2019). This control becomes particularly evident when examining the presence or absence of large predators, such as sharks. Still, it proves to be equally influential when the 'predators' in question are herbivorous grazers. When predators are removed from a given ecosystem, an

adverse domino effect often follows, commonly known as a trophic cascade. Trophic cascades will directly and indirectly result in alterations at all other trophic levels (Bierwagen et al., 2018). As this has become more prevalent over the past few years, it has quickly become apparent that the loss of apex predators and 'plant predators' alike is a serious global conservation concern (Boaden and Kingsford, 2015).

In coral reefs especially, a strongly influential factor in maintaining ecosystem balance through top-down control is the presence or absence of these herbivorous grazers. These grazers play a pivotal role in maintaining ecological balance primarily by providing space for young coral recruits to grow by limiting the expansion of rapidly growing fleshy algae (Williams & Polunin, 2001). Current research suggests that the presence of fleshy algae crowds out coral and beneficial algae, crustose coralline algae, alike (O'Leary & McClanahan, 2010). Coral is an essential component of a coral reef not just because of its aesthetic appeal, but because it creates structurally complex physical structures that support an abundance of niches which in turn support robust biodiversity (Jackson).

Selective grazer control helps CCA:

O'Leary and McClanahan (2010) explored the effects of top predator removal in a Kenyan coral reef ecosystem and how top predator removal affects primary production. Crustose coralline algae (CCA) is an important primary producer in coral reefs. Not to be confused with fibrous and fleshy species of algae, which in overabundance adversely affect coral, its presence is positively correlated with coral health. In general, the more grazers there are, the more CCA there will be. Grazers primarily take the form of sea urchins or fish with one of these groups maintaining dominance in a reef. In sites where fishing is prevalent, a phase shift can occur and a fish-dominated ecosystem may become overtaken by sea urchins as the primary grazers. Overfishing in these ecosystems creates a twofold effect: both the fish that compete with sea urchins and fish that prey on sea urchins are removed. In the study, sea urchin grazing was found to be more harmful to CCA than herbivorous fish grazing, creating an indirect yet strong correlation between the removal of top predators via fishing and worsening reef health.

Large commercially viable fish as top predators:

While overexploitation of fisheries is unambiguously a significant factor in ecosystem degradation, researchers in Fiji were able to investigate the exact effects of such an ecosystem disruption in the wake of a local fishery being mismanaged (Dulvy et al., 2004). As fishing intensity increased, reef predator densities decreased by 61%. Subsequently, coral-eating sea star densities increased by three orders of magnitude, while coral and CCA decreased by 35%. This decline in coral was matched by an increase in algae-dominated reef habitat, the algae working to further crowd out coral growth.

Parrotfish as mid-level grazers:

A Caribbean reef simulation study utilized parrotfish to investigate the impact of grazing on the ecosystem, especially when storms are factored into coral reef ecosystem disruption (Mumby, 2006). Parrotfish, acting as herbivorous grazers, influence coral-algal competition by grazing on the algae. The available habitat created through grazing allows coral to more easily reestablish itself after hurricanes. This proves sustainable if hurricanes affect a particular area once every twenty years and unsustainable if hurricanes affect an area once every ten years or more. Combined with the grazing effects of the sea urchin *Diadema antillarum,* however, coral cover was able to be maintained and remained relatively high (greater than 30%) during normal conditions. Yet in the face of complete grazer depletion, even if hurricanes occurred with a low frequency of once every sixty years, coral cover was predicted to rapidly drop to under 1% within a short period of time after. Even if grazing fish alone were restored, the simulation pointed to difficulty maintaining the reef in a grazed state without the assistance of *D. antillarum*, which faced a mass mortality event approximately forty years ago and has yet to recover.

Overfishing herbivorous grazing fish:

A 2014 study by Williams and Polunin supports these findings by exploring the direct relationships between macroalgae and the biomass of grazers. The grazers in this study included all present herbivorous fish and the sea urchin *Diadema antillarum.* They found a direct positive correlation between the presence of fishing activities and algal cover, suggesting that the overfishing of these mid-level grazers was indeed creating an environment in which coral struggles to survive and propagate. However, they found that fishing did not appear to entirely account for the overabundance of macroalgae found, with the high levels of macroalgae observed in lightly fished areas likely being a result of the absence of *D. antillarum.*

Nutrient Replenishment by grazers:

In a direct link between the importance of top-down grazing fish and the importance of bottom-up nutrient availability, a study in 2021 by Munsterman et al. found that the defecation of parrotfish and other herbivorous fish that were subsisting off of a coral-dominated ecosystem contained a higher nitrogen-to-phosphorus ratio than grazers in an algae-dominated reef. This higher N:P ratio appears to correlate positively with overall coral health.

Conservation Implications:

Identifying triggers for trophic cascades and recognizing their signs are critical for effective management. The vulnerability of top predators, especially in overfished areas, poses an existential threat to coral reef ecosystems. Overfishing overwhelms and immediately disrupts ecological balance, which in extreme cases leads to habitat destruction (Boaden & Kingsford, 2015).

The removal of herbivorous grazing organisms perhaps has the most direct effect on the coral itself within coral reef ecosystems. Overfishing is the primary force behind the loss of the herbivorous fish that are responsible for maintaining the low algal cover that is associated with high coral cover and higher reef complexity, the foundation of a healthy reef ecosystem that can support other organisms (Smith et al., 2010; Williams & Polunin, 2001; Jackson; Sandin et al., 2008).

However, overfishing is a wound inflicted on an otherwise already damaged system: in Caribbean coral reef ecosystems, the mass extinction of sea urchin *D. antillarum* is making it nearly impossible for herbivorous grazers to keep up with rapid algal growth even in unfinished states. Populations of *D. antillarum* plummeted in 1983, speculated to be caused by a water-borne pathogen (Lessios et al., 1984). Since then, the recovery of this species has been slow, with populations today being estimated at approximately 12% of what they were before the mass mortality events (Lessios, 2016). Immediate measures will need to be taken to support the restoration of this foundational species and create zones in which herbivorous fish can persist unfinished to maintain the ecosystem in the meantime. The establishment of no-take marine reserves is a start (Mumby, 2006), but effective restoration methods will need to look holistically at the specific functions of each consumer and the associated effects of their removal, both direct and indirect.

Bottom-Up Control in Coral Reef Ecosystems

Bottom-up control explores the intricate relationships between nutrient levels, microorganisms, and the organisms residing in coral reefs (Littler et al., 2006). In coral reefs, the 'bottom' involves nutrient availability and microbial processes as well as levels of primary productivity, all of which significantly impact the health of the entire ecosystem (Smith et al., 2010; Garren & Azam, 2011). Bottom-up processes directly support overall coral resiliency, perhaps the most critical trait to maintain in a time of great and unchecked environmental stress on corals (Garren & Azam, 2011).

Intersecting nutrient and herbivory levels:

A study in 2006 (Littler et al., 2006) cited the effects of eutrophication as one of the primary factors controlling the phase shift in coral reef ecosystems from coral and CCA-dominated to algal-dominated. Nutrients were found to promote algal growth (referred to here as fleshy algal growth), but varying levels of nutrients interacted with varying levels of herbivory (algae and plant consumption) in ways that changed the resultant ecosystem entirely. In general, increased nutrients led to increased algae growth. In their study, however, they found that even when nutrient levels were low, algae was not necessarily prevented from growing if herbivory was also low. The converse is also true: if herbivory is high, high levels of nutrients do not necessarily mean that algae growth increases. Combining these theories, high herbivory and low nutrients led to virtually no algal growth. This combination is ideal for sustaining a coral-dominated reef ecosystem.

Groundwater discharge as a microbial driver of phase shifts:

In yet another instance of a coral-dominated and algae-dominated ecosystem phase shift, Lapointe (1997) examined the excess nutrient availability in Caribbean algae-dominated coral reefs. In every location of the study, dissolved organic nitrogen (DIN) and soluble reactive phosphorus (SRP) were found to exceed their usual concentrations and surpass the required threshold for maintaining macroalgae blooms. The study found that DIN was associated with decreased local salinity, suggesting an influx of groundwater. Groundwater originating on land often comes laden with nitrogen-rich fertilizers, which promote blooms of algae and support algae-dominated reefs.

Coral Bleaching:

Perhaps the most salient and well-known example of bottom-up control in coral reef ecosystems exists within the corals themselves: the symbionts. These photosynthetic microorganisms work to provide the coral with food while they exist protected within the coral's calcareous skeleton. Yet like other microorganisms, when environmental stressors such as heat events or pollution are present, these symbionts are often ejected from the coral host (Douglas, 2003). It is the ejection of these symbionts from the coral that causes infamous coral bleaching (Mumby et al., 2006).

Theories as to why the coral willingly eject the microorganisms they rely on to live are founded in the idea that when given more energy– in the form of heat or extra nutrients, most often– microorganisms of any kind will be more productive. With increased productivity comes increased toxic waste products. As these waste products build up a greater rates than usual, the coral is harmed. It is hypothesized that in a last-ditch effort to protect the coral host's health, the symbionts are ejected (Baker et al., 2008). This drastically weakens the coral by leaving it vulnerable to malnutrition, disease, and death. When corals die or experience stunted growth, it decreases the physical complexity of coral reef ecosystems. High structural complexity in coral reefs supports a high biodiversity of fish, which supports all other trophic levels and ecosystem functions (Mumby, 2006).

Viral infections in coral:

Within the world of microorganisms exist the complex dynamic relationships between them, as explored in depth by Rosenburg et al. (2007). In addition to thermal stress, viruses can also cause coral bleaching disease, the most famous example of which is the bleaching of the coral *Oculina patagonica* by the pathogen *Vibrio shiloi.* While many of the mechanisms of virulence in this particular infection were induced by thermal stress (further highlighting the compounding negative effects of ocean temperatures increasing) the coral was eventually able to build up resistance to this virus, suggesting that an ever-evolving and adaptationally flexible coral microbiome is crucial to facing future environmental fluxes.

Conservation Implications:

Ecosystem resiliency becomes dramatically altered when, in the face of depletion of top-down and herbivory effects, bottom-up controls become the primary mode of trophic control (Littler et al., 2006). Eutrophication is a multifaceted issue, often the result of agricultural runoff but with many other contributing factors (Littler et al., 2006). Even if original levels of herbivory were to be partially or fully restored, the overabundance of nutrient pollution increasingly commonly seen in coral reef ecosystems will greatly hinder coral reefs' abilities to recover from stress events of all kinds (Littler et al., 2006). Increases in global ocean temperatures also engender difficult conditions for coral reefs: disease, symbiont rejection, and algal blooms are all supported by these warming seas (Jackson; Mumby et al., 2006; Ostrander et al., 2000).

Understanding the dynamics of nutrient availability, algal populations, and herbivory rates is crucial for devising effective conservation and restoration strategies to ensure the resilience and health of coral reef ecosystems.

Discussion & Conclusion

Across the current research, common threads of trophic control emerge, suggesting the degree of impact different trophic levels have on each other and, consequently, how coral reef health is intricately interlinked with every organism that inhabits them. While disruption of each tier exhibits distinct effects, several key variables are shared, underscoring the complexity of coral reef trophodynamics.

Notably, the algae population emerges as a central player, with direct connections both to nutrient levels and top consumers. The shifting balance between a coral-dominated reef environment and an algae-dominated reef environment becomes the working definition of the level of reef degradation. A loss of balance in any tier supports algae dominance and the crowding out of coral.

The obvious algae indicator is a central concept in many mitigation strategies. Studies propose that an increase in herbivore populations could potentially restore degraded coral reefs by directly managing overgrown algae populations. However, our findings here suggest that the issue is more complicated: this restoration strategy may only be effective in the absence or minimal occurrence of nutrient pollution, ideally in cooler-than-currently observed waters, and types of herbivores and the relative populations of each must be managed, highlighting the infinitely complex interplay between bottom-up and top-down controls.

On the conservation front, strategies considering any trophic level as unimportant to the others will likely not be effective. Given the interconnected nature of trophic controls, a comprehensive approach addressing both top-down and bottom-up influences may yield the most successful conservation outcomes.

At their core, all challenges facing coral reefs reviewed are anthropogenic. Overfishing, eutrophication, and a warming Earth are all viable threats to the continued existence of the ocean's most biodiverse biome. As it currently stands, the oceans are gradually and dangerously warming with no tangible plans to curb this increase. If these conditions continue, protecting top

consumers, implementing sustainable fishing practices, and addressing nutrient pollution and environmental stressors in controllable ways will be the most immediately viable options to promote coral resiliency in the face of inevitable heat events. Holistic, informed, and well-coordinated efforts must strive to collectively contribute to coral reef resilience and the hope of eventual restoration.

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"Finding America's Next Generation of Creative Thinkers: An Investigation of Competitions that Challenge High School Students to Embrace the Unknown" By Preston Chen

Abstract

America is built on innovation, and our current education system for high school students is not fostering the creative talent needed to sustain that innovation. Existing efforts to teach and to inspire creativity come in the form of project-based learning inside the classroom and various programs outside the classroom. Benefits in student academic performance, adaptability, and engagement are most profound when students participate in competitions that have open-ended and ambiguous challenges. This paper investigates how three specific student competitions at the middle and high school levels (American Mathematics Competition, Robotics, Debate) foster creativity through difficult math problems, steep engineering constraints, and impromptu rebuttals, respectively. Formalizing student participation in such settings will not only address the lack of creativity but also increase a much-needed sense of belonging among high school students.

1.0 Introduction

The United States has long been recognized as a hub of innovation and technological advancement, but how long can we keep that title? Since World War II, the US has built a reputation on the strength of its science and engineering graduate education (Teitelbaum). As the foundation of our evolution, this education system has been essential in producing technological advancements that boost economic growth, job creation, and standard of living. The intellectual contributions of our rising generation, especially from university and high school students, are the leading factor in maintaining this title. These students, often at the forefront of research and development in their academic institutions as they seek advanced degrees, are increasingly contributing to the pool of intellectual property (IP), which encompasses a wide range of disciplines, indicating a diverse and multidisciplinary approach to innovation (Babina).

The educational background of domestic patent recipients is notably credited towards higher education, with nearly 60% holding bachelor's degrees during the period of 2013 to 2017 (Fleming). Within this group, a significant 66% had degrees in STEM fields. Graduate degree holders, including those with master's (23%) and doctoral degrees (18%), are prominent in patent acquisition, accounting for 41% of U.S. patents (Fleming). This trend is further evidenced in university settings, where graduate students and postdocs (postdoctoral researchers who have completed their doctoral studies and are engaging in further training to enhance their professional skills) are predominantly responsible for university commercialization activities (Babina). The Bayh-Dole Act of 1980 plays a crucial role here, incentivizing universities to patent their research findings, thereby contributing to U.S. and global competitiveness.

The United States has benefited immensely from the contributions of international scholars and students, adding even more diversity and depth to its innovation ecosystem.

Increasingly, the source of key innovators has come from non-domestic talent, with immigrants making up 16% of U.S. inventors and being responsible for 23% of patents issued between 1990 and 2016 (Bernstein). Adding to the significance of immigrants to U.S. innovation, it's notable that these foreign-born inventors are numerous and highly impactful (Berstein). Their patents were slightly more influential, as indicated by the number of citations each received over three years, a key measure of patent quality and utility (Chen).

If a growing number of innovators are born in international countries, where does that leave the U.S. in terms of a talent pipeline? How can the U.S. continue to hold its title of the hub of innovation if all of its innovation comes from foreign minds? This review article aims to highlight current efforts to strengthen our domestic source of creative thinkers and recommends the next steps in achieving such outcomes.

1.1 Current trends in the American education system that limit student creativity and innovation.

The very foundation of the American education system, from kindergarten through 12th grade, is failing students when it comes to nurturing creativity and innovation. Journalist and chronicler of the rise of Silicon Valley, Po Bronson points to data showing "American creativity scores are falling... particularly for younger children in America—from kindergarten through sixth grade" (Bronson). This decline seems to be directly correlated to the overwhelming focus on standardized testing and rote memorization that currently dominates the education system in public schools. "There is no concerted effort to nurture the creativity of all children" amidst the focus on meeting curriculum standards that public schools are required to comply with (Bronson). Schools are so fixated on meeting requirements in order to receive funding that they compromise the quality of education for the students.

Psychologist Mark Runco's research at the University of Georgia has revealed an intriguing aspect of creativity in educational settings. His findings indicate that "significantly more creativity was reportedly displayed outside rather than in school" (Runco). The restrictive, structured environment in school appears to actively dampen the creative talents and potential that students possess. This is obvious in terms of engagement levels in the classroom versus creative pursuits and expressions outside of the classroom. Runco concluded, students have innate "creative potential. As evidenced by their creative activities and achievements outside of school, but these potentials are not displayed when they are in school, perhaps because usually there is more structure and restrictions in school" (Runco). While students possess creativity, the strict requirements of tasks presented in the classroom leave little room for personal interpretation and thus little room for creative thinking.

This rigid focus on standardized curriculum, rote memorization, and high-stakes testing is actively stifling creativity in students by prioritizing the passive absorption of information over encouraging original thinking, exploring interests, and innovating (Bronson). The result of this is that "As school stuffs more complex information into their heads, kids get overloaded, and creativity suffers" (Bronson). Overwhelmed students faced with the relentless pace of absorbing

and regurgitating facts lose the capacity to develop their own insights and ideas on the material. This unhealthy mindset of studying through memorization rather than interest essentially de-emphasizes education as a whole. What makes this crisis even more alarming is that advanced graduate programs are linked to increased innovation, competitiveness and economic growth for the nation (Leming). But realizing these benefits over the long term requires a more relaxed learning environment, one that is able to nurture creativity, curiosity and insight rather than de-emphasize the unknown and therefore failure. As Leming summarizes regarding graduate-level education, "sustaining quality training programs, retaining STEM experts, allocating research resources wisely, and applying new technical knowledge in translatable ways is equally vital" for ongoing innovation (Leming).

The emphasis on standardized testing and rigid curriculum in early education is failing to cultivate the types of creative minds that drive progress. Students overloaded with rote memorization are not quite equipped to solve unstructured problems they/humanity are likely to encounter in the future. Synthesizing information into original ideas and pioneering innovation in response to new crises are essential for the development and survival of humanity. America's traditional leadership in creativity and innovation is now threatened by this lack of emphasis on nurturing free-thinking students in the K-12 education system. Truly addressing this crisis would require recognizing the failures of the current system and taking steps in order to foster creativity and insight at every stage of learning. The passive, restrictive environment in most public schools actively inhibits the development of knowledge and capabilities that the modern economy increasingly demands. Currently, the students graduating from the K-12 learning system are not equipped to evolve alongside the face paced world of the present. How can we have robots/AI adapting to unforeseen problems when humanity can't do the same?

1.2 Fostering innovation in 21st Century through educational programs

Fostering innovation relies significantly on educational reforms and programs that emphasize creativity and critical thinking. Classroom training in creativity, mainly through experiential techniques, can greatly enhance students' critical thinking abilities and group skills, preparing them for careers in entrepreneurship/innovation (Shaheen). Integrating art and creativity elements into the STEM curriculum, evolving it into STEAM (Science, Technology, Engineering, Arts, and Mathematics) programs, equips students with advanced problem-solving skills and technology fluency necessary to adapt to the future of job markets (Chicas). Looking at existing examples, nations like Singapore, Finland, and South Korea demonstrate the impact of education investment reforms with their increased innovation capacity and global competitiveness (Han). Such reforms are not just about enhancing academic performance, but about shaping a workforce capable of innovation and adaptability in a rapidly changing world. This approach includes both project-based learning within classrooms and reinforcement learning—a combination of scholastic and practical experiences—alongside various extracurricular programs that further nurture creativity and innovation outside the traditional classroom setting (Shaheen).

Programs outside the classroom that emphasize competition have taken the lead in fostering innovation and creativity by nurturing high-ability students. These competitions, such as the American Mathematics Competition (AMC), team-based robotics and high school debate, serve not only as platforms for talent identification and development but also as catalysts for enhancing the educational process itself. The common theme in all these programs is ambiguity. Open-ended problems and challenges allow for students to really flourish as individuals, thereby encouraging students to shape their own education rather than having a teacher shape it for them. The benefits in student academic performance, intellectual adaptability, and learning engagement are profound when more is demanded of them. What follows is a summary of the literature on these programs as case studies for fostering creativity.

2.0 Case Study #1: The American Mathematics Competition

Mathematics competitions such as the American Mathematics Competition (AMC), play a crucial role in identifying and fostering high-ability mathematical/creative thinking students. These benefits impact not only individual participants, but also educational institutions, and the field of education itself. The integral role of mathematics competitions like the AMC in nurturing high-ability students in mathematics and creative thinking benefits individuals and enhances educational systems.

2.1 Identification and Fostering of Talent. Competitions are crucial in identifying students with exceptional ability of any kind. As noted by Kenderov, "Competitions help identify students with higher abilities in mathematics [and] . . . develop their talents and to seek professional realization in science (Kenderov)." When competing against classmates, friends, and peers, students are pressured to perform to the best of their ability, helping educational institutions to see the full extent of their students abilities. In comparison students that only seek education in the classroom often lack the challenge needed to unlock their true potential.

2.2 Positive Impact for Schools. The influence of competitions extend beyond just individual participants and actually benefits academic institutions as well. By spectating competitions and study skills that challenge students, teachers can learn improved teaching methods, and have a heightened interest among students that desire to be challenged. Schools can take advantage of this by teaching skills and introducing problems that leave students searching for an answer rather than being handed it.

2.3 Benefits For All. The advantages of mathematics competitions and competitions in general is the rewards are not limited to just the winners. As Kenderov points out, "What frequently escapes public attention . . . is the fact that the other, 'non-winner' participants, also gain a lot" (Kenderov). Even without standing out due to exceptional capabilities, the non-winners gain knowledge that helps strengthen their individual skills. Studying for a topic that's not your strong suit can show you the best way to learn which is unique for every individual. By taking the competitions and thus preparing for them, students gain the skills needed in order to excel in other aspects of their life whether it be another academic topic, sports, or social interactions (Kenderov).

2.4 Development of future mathematics curriculum. Through the ever changing nature of mathematics and mathematical competitions specifically, this guarantees the continuity and advancement of difficult mathematical knowledge that best suits our modern world. "A significant part of the classical mathematical heritage known as 'Elementary Mathematics' is preserved, kept alive and developed through the network of competitions and competition-related activities," which also allows for the adaptation of new mathematical concepts that best fit our world today while still building on the fundamental basics (elementary mathematics) taught for centuries (Kenderov).

2.5 Preparation for future. Similarly to the point that Kenderov makes about the benefits of competitions for all is reinforced by Susnea who states, "Competition based learning (CBL) is beneficial not only for the relatively small group of winners – the other, non-winner participants have also a lot to gain as preparation for future real-life competitions" (Susnea). Competitions with settings similar to the AMC focus on reactive thinking and prepare students with a set of skills that enables them to think without telling them what to think. Other than learning a set of basic fundamentals like notations and strategies, the only real preparation is through repetition. Requiring students to prepare by engaging in difficult open-ended problems and taking tests multiple times after only receiving scores like a 4 out of 25 emphasizes the dedication it takes to reach any goal in life. After receiving a low/undesirable score on the AMC, students must learn to take away from that experience and take another test, often receiving the same score and sometimes even a lower one.

2.6 Adapting to future challenges: the evolving nature of competitive mathematics. The nature of competitions inspires subsequent competitions to implement practices learned from the prior (Losada). Once again, it's important to understand the flexibility of competitions as an educational opportunity. They allow for tests to adapt from one another and can change based on the educational standard of the ever evolving world. Seen each year, the AMC continues to grow in difficulty which emphasizes the need for more creative/reactive thinkers in order to prepare humanity for AI and all the complications that come with it. Modern challenges might include unforeseen breakthroughs or challenges in AI that need fast solutions such as information hacking that is inevitably going to evolve along with AI.

2.7 Boosting confidence and growth: the psychological benefits of competitions. Losada also emphasizes that competitions can be particularly beneficial in boosting the self-confidence of students, a quality that is often lacking in newer generations. Competitions address the problem by forcing students to see their own true potential in competing thus giving them a sense of confidence (Losada). Even the students that don't excel at their current competition can learn from the process in which they competed, taking their newfound experiences into a different field in which they excel. Everyone has a competitive side, emerging when seeking to prove oneself which activates the true potential of a student that is required for great success (Susnea). Through competition, students can practice this mentality and hone it in order to use it in other aspects of their lives.

3.0 Case Study #2: National Robotics Competitions

Robotics in education has been recognized as a tool for enhancing student learning, especially in the realm of STEM (Science, Technology, Engineering, and Mathematics). Robotics, due to its multifaceted nature and its ability to develop cognitive and social skills, has recently increased in popularity among students and teachers (Afari & Khine). A key aspect of educational robotics is the nature of its interdisciplinary approach, which includes mathematics, physics, design, innovation, electronics, computer science, programming, and psychology (Afari & Khine). This multi-educational aspect not only diversifies learning, something essentially for young adults, but also prepares students for the complexities needed in real world problems and occupations.

Robotics programs such as the VEX Robotics Competition, FIRST Robotics Competition, FIRST Tech Challenge, and FIRST Lego League are available throughout the US and the world. Started in 2007, VEX programs in 2022 involved over 400,000 students in grades 4-12, and about 30,000 students from more than 50 countries participated in their annual robotics world championships (REC). Since 1989, FIRST Robotics programs have seen more than 2.5 million student participants from 100 countries, and approximately 668,000 students participated in the 2022-2023 season ("At-a-Glance"). Its programs are organized by age group, with the challenges and technical demands increasing in difficulty as the student ages. In 2022, FIRST Robotics had its annual international competition with participation from 3,225 teams, including more than 80,000 students and 25,000 mentors from over 26 different countries ("At-a-Glance"). This level of participation for these programs shows this field's popularity and international importance.

3.1 Reinforcement learning in robotics. Another key aspect of robotics is its relation to the constructivist theory of learning, a type of learning that emphasizes learning through hands-on involvement through things/activities that hold personal significance (Eguchi). The nature of robotics forces students to innovate, which almost always stems from a place of need. When someone desires something that is not given, they are inclined to seek it out themselves, this is the key educational aspect of robotics. Educational planners globally are recognizing the potential of robotics, leading to its semi-recent integration in school curricula to offer students of all ages the opportunity to learn with robots (Afari & Khine). Programs like RoboCupJunior, for instance, stand out for their effective promotion of STEM learning, as evidenced by studies that highlight RoboCupJunior as an influential educational robotics program (Eguchi). These programs provide project-based and goal-oriented learning experiences with lasting impacts on student motivation and interest in STEM fields (Eguchi).

3.2 Statistical influence of robotics on education. The influence of robotics education on student lives is also noteworthy. According to Melchior, participation in robotics programs like FIRST Robotics is associated with higher rates of high school graduation and college attendance (99% of FIRST alumni in the study graduated high school compared to 65% nationally, and 89% attended college compared to 62% nationally). There's also a notable increase in the pursuit of STEM careers among these students, with a significant percentage

majoring in engineering in college (41% of FIRST alumni majored in engineering about 7 times the national average of 6%) – far exceeding national averages. This trend is particularly encouraging for female and minority students, who have shown higher rates of pursuing engineering majors compared to national averages (Melchior).

        3.3 Rationale for implementing robotics programs. Educational robotics doesn't just enhance technical skills; it also fosters critical thinking and problem-solving abilities. Studies cited repeatedly by authors like Okita, Kim, and Mohr-Schroeder demonstrate the positive effects of robotics on students' engagement in STEM, proportional reasoning skills, and understanding of mathematics and physics. Besides its benefits, robotics is also incredibly user-friendly and has enabled teachers, even those without strong backgrounds in robotics or programming, to incorporate robotics/STEM learning into their classrooms (Oppliger). The popularity of the subject has led to an increase in online material, making it easy and cost-effective for scholastic programs to reap the benefits of robotic education on students.

4.0 Case Study #3: Debate Competitions

        Debate fosters critical thinking, reasoning skills, and social-emotional skills. Students who engage in debate are constantly challenged to explore open-ended questions, which encourage them to think beyond mere surface-level education often required by schools (Bauschard & Rao). This leads students to deal with diverse information when researching as well as forces them to create sound logical arguments to the common parent which sharpens their flow of thinking (Bauschard & Rao). By evaluating different aspects of an issue, students in debate learn to make informed, rational decisions, a critical skill that benefits all students beyond the educational surface.

        4.1 New perspectives and social-emotional learning. Debate also plays a crucial role in fostering empathy and social tolerance in young students (Bauschard & Rao). As students delve into their side of an argument (which is assigned to them), students will often find themselves defending a side that is not their own, and attacking a side which is. This leads students to understand the perspective of opposing viewpoints beyond just debate. This promotes empathy and understanding, an important aspect of collaboration and creating more interconnected communities (Bauschard & Rao). Debate also de-emphasizes verbal aggression, something that often takes away points in a competition. This promotes more civilized arguments which is something not really seen in the modern political world today (Bauschard & Rao).

        One of the key benefits of competitions in general, as pointed out earlier, is addressing the lack of confidence in younger generations (Losada). Debate perfectly answers this issue as the main aspect of debate is persuasiveness. Participants must be 100% confident in themselves and in their argument in order to convince someone else to believe in their points (Parcher). This deals with both preparation and confidence in one's own skills. Students often deal with 20+ hours of preparation each week (Bauschard & Rao) in order to develop their argument and combat counter arguments. It's clear that if both sides of a debate arrive this prepared, the decision comes down to which of the participants is more persuasive and cunning (Parcher). In

the opening both students must have utmost confidence in their argument which is often a prerequisite to performing in high level debate. Once the debate enters a more argumentative aspect, students must absorb information fast, decide on a point of attack, and narrow in on the weak aspects of their opponents argument. Students back out of an attack as that shows lack of confidence, thus proving their opponents' arguments are flawless.

4.2 Skills developed through competition-oriented debate programs. Critical thinking, communication, and performance are all academic benefits that once again are exercised in debate. Students who participate in debate tend to perform better academically, as the skills acquired are transferable to various academic disciplines and learning situations (Bauschard & Rao). The nature of debate, which requires a variety of skills including but not limited to, economics, philosophy, and political science. This grants students a more holistic and modernized education rather than the traditional math, english, history, and science as taught in schools (Bauschard & Rao).

The nature of discussing varying political and economic issues around the world often leads students to heavily research beforehand. This exercises a number of academic practices crucial to modern education yet not taught in schools (Hogan). First is independent research. Schools often include small aspects of research in classes like history, yet their research is guided. In class students are given a website, sometimes a link and asked to essentially translate the source online into a doc. In debate students must independently find sources, consider whether or not they are trustworthy/verified, and turn those sources into well flowing debates that both support their points and attack the other. Forcing students to learn research skills is a crucial part of adult life which requires humans to find solutions to their own problems (Hogan).

Another benefit of debate for highschoolers is that it's preparation for the future. Eldred emphasizes that effective communication is a highly sought-after skill across various fields. Employers prioritize oral communication skills in potential employees. This is where debate, with its focus on audience adaptation, clear speech, and logical persuasion, excels. Debate encourages debaters to engage their audience with eye contact, an open body position, and varied vocal delivery (The Triangle Method). Such skills are essential in the real world, where the majority of message meaning is often conveyed nonverbally.

5.0 Recommendations

In the wake of the pandemic's profound impact on education, now is a better time than any to implement these educational programs. The pandemic has, without a doubt, brought trauma, loss of resources, and unequal impacts on underserved communities (Kuhfeld). However, the shift to online learning comes with an opportunity to overcome geographical and socioeconomic limitations, making these programs more accessible to a diverse student population. The timing for starting or enhancing these programs is perfect, as they not only offer a solution to the intellectual and social isolation caused by the pandemic but also equip students with critical skills needed in an increasingly digital and interconnected world. Implementing these competition-oriented programs offers numerous benefits, fostering important life skills

such as effective communication, critical thinking, and confidence in working collaboratively. Implementing now is an investment in students that goes beyond academic achievement, by preparing students for future challenges in higher education and their careers.

5.1 Implementing the American Mathematics Competition (AMC). This is by far the hardest program to implement due to the high educational requirement to teach the subject as well as minimal online resources that provide curriculum. Team fees can cost around $10-30 per student combined with mentor costs, usually around $1500-3000 per mentor. Given the costs associated with team fees and mentor expenses for implementing AMC-level educational programs, schools should consider sponsors from local businesses/academic programs or explore other reinforcement learning implementations listed below.

However, if funding is not an issue, a structured approach is needed in order to have a successful implementation of AMC mathematics. Firstly, awareness about the competition should be increased through informational sessions and promotional activities, ensuring students understand the benefits and opportunities it offers. Schools should then provide resources for preparation, such as access to past AMC papers and problem-solving workshops. This can be facilitated by math clubs or dedicated AMC preparation groups patterned after programs like UCI Math Community Educational Outreach Program (UCI Math CEO) or Los Angeles Math Circle (LAMC), both of which aim to extend the influence of open-ended mathematics to the general public (MAA & Santillanc).

Moreover, it's crucial to involve mathematics teachers in the process, enabling them to integrate AMC-style problems into their regular curriculum, which can help students adapt to the competition's format and difficulty. Collaboration with local universities is also an incredibly helpful option as it can sometimes fulfill the high education requirement in order to teach the subject. Finally, establishing a supportive environment that encourages participation and celebrates effort, regardless of winning, is essential for the sustainable success of the AMC program. A reminder that the AMC 8,10, and 12 are incredibly difficult tests, often yielding a score of 6.13/25 or a 24.52%. Results like these will be new to a majority of students and it's important for low scores to not hamper their future participation. Participating in the AMC will nurture students' critical thinking and problem-solving skills, providing them with a valuable foundation for academic success and future endeavors.

5.2 Implementing High School Robotics Programs. For the effective implementation of high school robotics programs, a multi-faceted approach is necessary. Initially, securing funding and resources is crucial. Unlike AMC, online resources are incredibly abundant; however, the materials required to source a robotics team is quite expensive. Programs at the elementary and middle school levels start around $1500 (FIRST Lego League) and progress to $5000 (FIRST Tech Challenge) to $25,000 (FIRST Robotics Competition) per season. These costs could be tackled through sponsorships from local businesses, technology firms, educational grants, or school fundraisers.

Next, schools should focus on building a team of enthusiastic teachers and mentors, possibly including professionals from the field of robotics, to guide and inspire students.

Hands-on workshops and regular team meetings are vital for practical experience. Schools should also create opportunities for students to showcase their work, such as internal competitions or exhibitions, which can foster a sense of community and teamwork. This is important as showcasing work to the local community can bring in more attention which means more resources and participation. Moreover, integrating robotics into the existing curriculum, even at a basic level, can pique interest across the student body.

Networking with other schools to share resources and experiences can also enhance the program's effectiveness. Robotics often requires the help of a big part of the community which often leads to the community's role in the program. This could not only prove to be beneficial for students and their futures, but also for the schools and families nearby.

5.3 Implementing High School Debate Programs. Implementing a debate program in high schools, similar to the previously stated programs, can be a challenging but invaluable addition to the educational experience. While they may not have the high technical requirements of the AMC and robotics, debate programs likewise require careful planning and resource allocation. Firstly, the cost of establishing a debate team can vary, but schools should anticipate expenses varying from $10,000-20,000 on entry fees, judge fees, and coaching fees (Debateus). These costs can be offset by seeking sponsorships from local businesses, educational institutions, or school fundraising efforts.

Awareness and interest in the debate program can be raised through informational sessions and promotional activities, highlighting the skills and opportunities debate offers, such as enhanced critical thinking, public speaking, and research skills. Schools should provide resources for training and practice, including access to debate materials, workshops, and experienced mentors. Collaborations with local universities or debate organizations can offer additional support and expertise.

Creating a supportive and inclusive environment is crucial. Students should feel encouraged to participate regardless of their skill level, and efforts should be made to ensure that all interested students have the opportunity to join. Finally, it's essential to manage expectations. Debate competitions can be challenging, and students will often face competing students with years of experience. Emphasizing learning and growth over winning is key to maintaining student engagement and enthusiasm.

Conclusion

Competitions like the American Mathematics Competition, Robotics, and Debate foster innovation and creativity rarely found inside classrooms. These platforms not only challenge and nurture young minds but also contribute significantly to their academic and personal development. Emphasizing the need for more real-world applications and creative problem-solving in education, this paper advocates for integrating such dynamic and engaging learning experiences into the curriculum to prepare students for future challenges and maintain America's status as a hub of innovation.

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The Semiconductor Supply Chain: Implications for China, US, and Taiwan Relations By Anaya Tsai

Introduction

The semiconductor industry is one of the most important industries in the world, not only due to the immense applications of advanced computer chips to modern technology, but also due to the implications of the industry on geopolitics. Semiconductors ("chips") are used in almost every sector of electronics and enable advancements in healthcare, military systems, transportation, clean energy, artificial intelligence (AI), and countless other areas. The semiconductor industry is one of the most complex industries in the world and annual sales totaled more than half a trillion dollars in 2022 (Thadani and Allen 1-2).

This essay specifically looks at the implications of China's position in the semiconductor supply chain (SSC) on the country's relationship with the US and Taiwan. The SSC encompasses many complex processes that rely on geographic specialization. As a result, it is susceptible to disruptions caused by small policy changes or resource scarcities. There are six key players in the supply chain: The US, South Korea, Japan, Taiwan, China, and Europe (Khan et al. 3). Out of these six, the relationship between China, the US, and Taiwan is especially interesting as it fits into a larger discussion about the future of the post-war global economic order.

In the last two decades, trade between China and the US, two of the world's largest economies, has significantly increased. While such trade has been mutually beneficial, it has also led to increased economic tension, culminating in the China-US trade war in 2018. The trade war has already pervaded the semiconductor industry in the form of the US regulations on exports to Chinese semiconductor companies (Allen 1). While China and Taiwan also harbor economic and political tensions, the relationship of the Cross-Strait countries is very different to that of China and the US. China and Taiwan's relationship is uniquely rooted in historical and ideological beliefs about unification. Nevertheless, the economic implications of their relationship should not be diminished (Sacks).

This essay will first analyze China's advantages and vulnerabilities within the supply chain, including data on China's market share in specific sectors and government policy. It will then draw out to the international sphere, first analyzing China and the US's relationship within the supply chain and later China and Taiwan's. The analysis will end with an assessment of the weakness and existing problems in the SSC and draw conclusions about the effects of the semiconductor industry on the triangular relationship between China, the US, and Taiwan.

Analysis

The Semiconductor Supply Chain is driven by research and development (R&D) which underpins all three of its main sectors, design, fabrication, and assembly, test, and packaging (ATP), as shown in Fig. 1. These steps can happen in a single firm, an integrated device manufacturer (IDM), or in separate firms where fabless firms design the chips, foundries fabricate them, and outsourced semiconductor assembly and test (OSAT) firms provide ATP

services. Design is largely composed of two elements: electronic design automation (EDA), the software that designs chips, and core IP, the reusable modular portions of designs. Fabrication utilizes materials and semiconductor manufacturing equipment (SME) to turn designs into chips. Semiconductor fabrication facilities (fabs) use wafers to make the chips. The third sector, ATP, is the back end of the SSC and involves cutting a finished wafer into separate chips and packaging it to be used in external devices (Khan et al. 3-4). While this is a simplified explanation of the very complex production process, it is important to note the basic tenets of the supply chain in order to understand China's position within the industry.
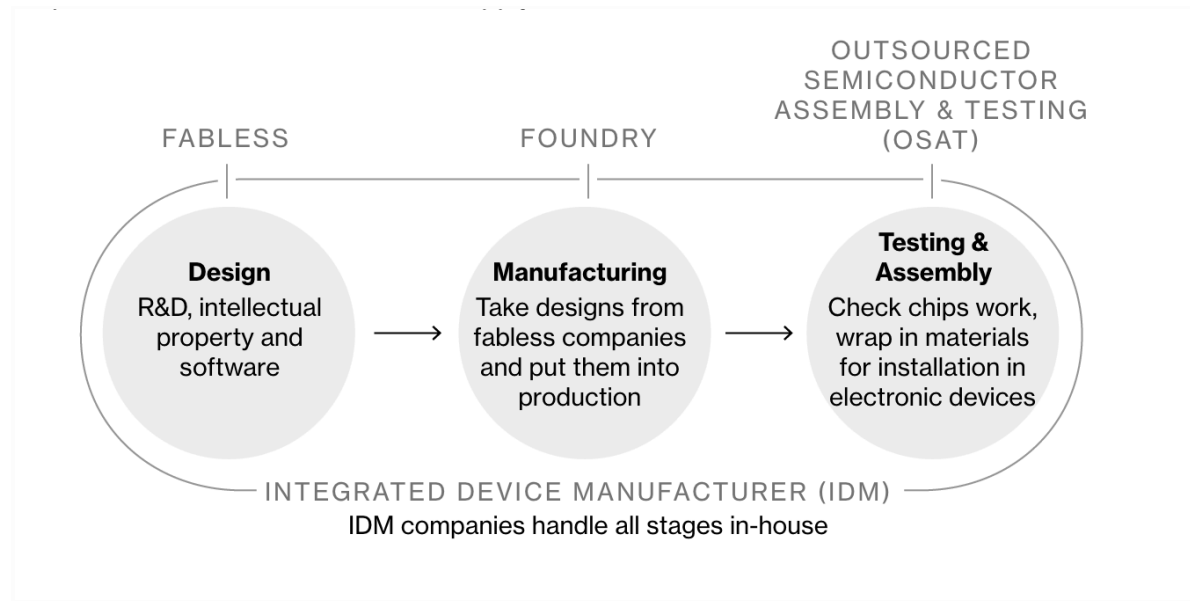
Fig. 1. "Semiconductor Production"

In the past, China has had the most success in the ATP sector due to its government infrastructure and workforce. In 2021, China accounted for 7% of the total $555.9 billion semiconductor sales, the majority of which come from China's ATP firms (Thadani and Allen 2). China has the most ATP factories in the world, comprising 134 of the total 484 ATP factories in 2021 (Thadani and Allen 11). While ATP is critical to the supply chain, it is the least technologically advanced and research dependent sector, thus making it a smaller market than fabrication or design. China's success in labor intensive, rather than research intensive, sectors can be explained by its large supply of cheap skilled labor. China has three large packaging and testing firms: Jingsu Changjiang Electronics, Tianshui Huatian Microelectronics, and Tongfu Microelectronics. Interestingly, all of these companies are rooted in state owned electronic factories which were privatized in the reform era, relating China's historical economic reform to its success in the modern industry (Li 128-129).

China's achievements in the SCC can be partially attributed to the government infrastructure which has facilitated the country's technological rise. A large shift occurred in China's chip industry in 2001, after China entered the WTO and leading international firms

started to open local operations. Five years later, China adopted "indigenous innovation" as its national strategy in the technology industry. This strategy launched 16 National Science and Technology Major Projects ("Mega Projects") in important sectors, several of which applied to semiconductors (Li 125). Following the early 2000s, the Chinese government continued to operate large scale programs and funding plans dedicated to advancing its semiconductor industry. In 2014, the government established the National Integrated Circuit Investment Fund (National IC Fund), which aimed at comprising $150 billion in investments from central and provincial governments to ensure that at least 70% of semiconductors consumed by China were produced domestically. In 2015, the Chinese government also announced "Made in China 2025," a $300 billion plan aimed at making China a manufacturing leader in 10 industries, including semiconductors (Ezell 17-18). Both the National IC Fund and "Made in China 2025" fit into China's broader strategy of utilizing state ownership and government subsidies to encourage investment in the semiconductor industry. Both plans have also resulted in increased outbound and inbound foreign direct investment, helping Chinese companies integrate further into the global supply chain.

Despite the scope of China's government plans and subsidies for the SSC, China is not a leading producer in design. Consequently, Chinese firms often depend on other international companies' design technology and do not pioneer technological advancements. This leaves China's semiconductor industry especially vulnerable to economic sanctions. While China acquires a substantial amount of design revenue every year, Chinese fabless firms cannot compete on a technological level with American design firms. Out of the total $13.3 billion in global IC design revenue in 2021, China accounted for 7% (Thadani and Allen 3). This percentage may seem high, but China's EDA industry is relatively small, and only one company, Empyrean, can run a complete design flow. The rest rely on design tools from the US and the UK, evident as 95% of Chinese semiconductors use core IP from ARM, a UK firm (Khan et al. 50-51). Core IP and EDA determine the efficiency and effectiveness of semiconductor design software. Therefore, having advanced production capabilities is critical for a country to lead semiconductor design.

Within the fabrication sector, China accumulated 15% of the total $44.7 billion wafer fabrication materials sales and 2% of the total $108.5 billion semiconductor manufacturing equipment market share in 2021 (Thadani and Allen 4-6). Therefore, while China does not have a large role in equipment manufacturing, it does supply many firms with necessary materials. China also has potential to expand further into fabrication as it already has a successful foundry: the Semiconductor Manufacturing International Corporation (SMIC). SMIC is the fifth largest foundry in the world, following companies such as Taiwan's TSMC and the US's Intel. China is also actively pursuing the development of more fabrication facilities, and it is estimated that China will have 28 new fabs operating by 2025 (Thadani and Allen 9). Within fabrication, China's weakness is that it still relies on foreign SMEs. In 2021, China purchased more than $28 billion of SMEs, making it the largest market for such equipment in the Indo Pacific (Thadani

and Allen 8). Therefore, dedicating resources to limiting China's dependence on foreign suppliers will be critical for China to assume a larger role in the semiconductor industry.

Unlike China, the US is a leader in the advanced technology sectors of the SSC, notably design. Part of the US's advantage over China is that South Korea, Japan, Taiwan, and Europe are all its allies. In contrast, China's political relations leave it vulnerable, as shown when other allies backed the US's recent regulation of Chinese companies. The US's achievements in the semiconductor industry are largely due to the country's leading role in R&D. In 2018, $64.6 billion was spent on R&D within the semiconductor industry. The US spearheaded this research, spending $39.8 billion. In contrast, China only spent $2.6 billion in the same sector (Khan et al. 12). The US also leads the design sector comprising more than 40% of the global IC market share, including EDA and core IP (Thadani and Allen 19). The US's largest fabless firms, which are responsible for design services, include Nvidia, Broadcom, and AMD (Alsop). In 2021, it was estimated that the US made up more than 70% of the $8.27 billion EDA market. This advantage is critical to its success in the SSC because design software is highly concentrated. Thus, the US has been able to leverage its EDA market, introducing export controls on US companies supplying EDA software to Chinese firms. The US is also a large supplier of equipment and accounted for 40.9% of the $109.5 billion SME market in 2021 (Thadani and Allen 4-6). As the US is a leader in manufacturing software and equipment in the supply chain, it is the primary supplier to many countries abroad.

When analyzing China and the US's relationship, it is important to note that China functions both as a consumer and a competitor. China is one of the largest markets for semiconductors in the world, importing more than $300 billion of semiconductors and comprising at least 25% of the US's sales (Thomas). A key example of China's consumption of US products is in wafer fab equipment (WFE). The US makes up 44% of the global market share for WFEs, and consequently, over half of China's equipment comes from the US. China's dependence on American WFEs has already increased in the last 4 years. In 2017, the US revenue from WFE sales to China was $3.7 billion; however by 2021, it was $12.4 billion (Thadani and Allen 8). This revenue will only increase if China wants to advance further into fabrication and cannot domestically manufacture the necessary equipment. Therefore, China would still be supporting the US's equipment industries while trying to compete with the US's fabrication firms. It is important to note that China's role as a consumer is central to its advantages and vulnerabilities in the supply chain.

As China and the US's mutual dependency in the SSC grows, so does the opportunity for regulation. On October 7, 2022, the US government announced new controls on exports of AI and semiconductors to China. The export controls aim at limiting China's access to high end AI chips and design software as well as the equipment needed to domestically produce such chips. Under this policy, large companies such as Nvidia and AMD are required to gain a license from the Department of Commerce in order to export their products to China (Allen 2-3). The US's allies in the chip industry have also enacted restrictions following the US export controls. For example, in May of 2023, Japan announced restrictions limiting China's access to older chips in

addition to modern ones. The US regulations had previously blocked more advanced chips; however, Japan's controls blocked simple chips used in everyday products, such as cars (Yang). While it is expected that new regulations will threaten China's production of semiconductors and force the country to turn to alternative suppliers, the larger question is whether the export controls are enough to disrupt the broader supply chain. In 2021, the US also enacted export controls; however, Chinese firms unexpectedly grew. Empyrean, China's largest design company, offered its technology at below market rates and became a partner of the advanced foundry ecosystem of Samsung, South Korea's largest IDM firm (Thadani and Allen 4). Therefore, analyzing the future effects of US export controls will be critical to better understanding the intricate web of the SSC.

Taiwan's success in the supply chain is even more concentrated than that of the US and is largely credited to a single fabrication firm: the Taiwan Semiconductor Manufacturing Company (TSMC). TSMC is the world's largest foundry, and its capacity to produce advanced chips renders Taiwan a critical player in the supply chain. In 2019, Taiwan accounted for 60% of foundry market shares (Khan et al. 20-22). While China also has several large foundries, Chinese firms do not generate the same international demand as Taiwanese companies, due to their inability to produce the highly advanced technology, such as 3 nanometer nodes. 3nm nodes are more effective than larger ones and spur new developments in artificial intelligence and national security. They are also extremely costly and research demanding. In 2021, TSMC estimated that it cost at least $20 billion to produce a 3 nm fab (Thadani and Allen 9). Therefore, despite increased government investment, it will be very hard for China to completely overtake Taiwan's central position in semiconductor fabrication.

Within the global network of fabs, country ownership is complicated by the fact that many IDMs and foundries have factories operating in other countries. For example, in 2022, American and South Korean firms each operated 11 fabs in China. Taiwan even had 13 facilities in China. It is important to note that internationally operating fabs tend to have less manufacturing capability because more advanced fabs are kept within the firms' countries. However, internationally operating fabs are subject to change, and in light of the US's new export controls, many experts believe that the US and its allies will start to move fabs out of China (Thadani and Allen 11).

Taiwan's advantages in semiconductor fabrication have solidified its economic relationship with the US. The US's largest tech firms, including Apple, Amazon, and Google, source almost 90% of their chips from Taiwan-based manufacturers (Arcuri and Lu). A result of this close economic relationship is that Taiwan was also affected by the US's 2022 export controls. It is estimated that US sanctions halved TSMC's exports to China, which now accumulate 10% of global sales (Mark and Roberts 9). The US also views Taiwan as a critical ally to ensuring its dominance within the SSC, and thus has been pushing Taiwan to "pick a side." Scholars connect this effort to TSMC's $40 billion investment to establish a fabrication facility in Phoenix, Arizona in 2021 (Mark and Roberts 4). Many people believe that this factory

is not a smart investment for TSMC and instead view it as a means for Taiwan to align itself with the US as the Cross-Strait tensions increase.

As shown by the analysis mentioned above, the post-pandemic climate has led to a series of new investment projects and regulations backed by geopolitical interests between China, the US, and Taiwan. Increasing friction within the SSC can partially be attributed to the global semiconductor shortage that started in 2020, during which the revenue projection of the industry decreased by $55 billion. The first, and most obvious, catalyst for the shortage was COVID 19. The combination of an increasing demand for semiconductors, the shutting down of chip manufacturing facilities, and disruptions in chip transportation accumulated in a semiconductor deficit. This deficit exacerbated already existing weaknesses within the supply chain: the process's complexity and geopolitical issues. From 2019-2020, Japan and South Korea were trying to mitigate a series of regulations and court rulings against businesses, while the China-US trade war escalated. Both conflicts introduced trade regulations that worsened the effects of COVID 19 on the supply chain (Mohammad et al. 481). These weak points of the SSC will become even more important in the future as the applications of chips continue to grow.

Conclusion

As semiconductors have proven to be critical to governments, citizens, and scientists across the world, key players in the SSC are leveraging their advantages and addressing their vulnerabilities. Semiconductor policy is also becoming more integral to international political relationships. Take, for example, China's long standing ideology about unification with Taiwan. In the past, Taiwan's centrality in the fabrication sector has served as a deterrent for China's attack. However, if China can achieve a high level of domestic fabrication capacity, the significance of Taiwanese fabs as a "silicon shield" decreases. Given China's current advantages with SMIC and abundant government incentives, it is likely that China will be expanding into fabrication, although the degree to which is still unknown. The US also functions as a deterrent for China's attack due to its prominence in design. If China were to attack Taiwan, the US would further cut off China's access to design software. As fabrication and ATP both rely on design software, China would face shortages in critical semiconductor supplies. Therefore, it is unlikely that China will attack Taiwan until it can ensure access to design and fabrication through increased domestic production capabilities.

The large losses at stake in this situation also suggest that the Chinese government may be further ahead in the semiconductor industry than publicly known. While China has already published several plans to further invest in the design and fabrication sectors, the capability of such firms to develop advanced technology is still unclear. In addition, China's command economy makes it easy for the government to direct funds into sectors in need. Regardless of how much information is available or not, it will be critical to understand China's developments in design and fabrication, especially when considering the risks of invasion for Taiwan. As a potential China-Taiwan-US conflict poses huge threats to the entire global economic system, the

significance of China's development potential in the semiconductor industry should not be understated.

Further research should also be devoted to understanding the impact of US export controls. It will serve every key player's interests in the SSC to better understand the weakness of the supply chain as a whole, especially in light of the recent chip shortage. Between China's growing investment, the US's new regulations, and Taiwan's complicated relationship with both countries, there is a tremendous amount of activity in the SSC. Thus, semiconductors will undoubtedly become even more important in the future both to technological advancements and global politics.

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Christian Churches in South Korea: An Analysis of Their History During the 50s to 70s Under the Lens of Anti-Communism By Yeso Lee

Abstract

Christianity is often credited with the process of democratization in South Korea, being touted as a force of social good. Although this claim holds merit, this paper will focus on complicating this narrative. This study, focusing on Christianity in South Korea from the 1950s to the 1970s, will take on a comprehensive view of Christianity and its relationship with both the regimes of Rhee Syngman and Park Chung Hee. The paper will complicate the dominant historical narratives echoed in contemporary Korean society by highlighting the other side of Christian political and social intervention. The paper first highlights relevant historical contexts, underscoring the nation's early history, the characters of Rhee and Park, along with a brief history of Christianity in South Korea. Then it examines the relationship between the Rhee regime and Christianity through the lens of anti-Communism. The paper will seek to highlight how Christianity's fixation with anti-Communism helped Rhee establish his political authority, a fact often disregarded by scholars. Afterward, the paper will connect the relationship between Rhee and Christianity to the relationship between the Park regime and Christianity, emphasizing, once again, how the Christian fixation with anti-Communism led to the support of another dictator. The paper will then focus on the dominant historical narrative, which claims Christian support for the democratization of Korea and the downfall of the Park regime, and how it fits into this new narrative. Finally, the paper will argue that such religious dynamics be analyzed within a systematic historical and social context.

Introduction

The Gwangju Protestant Community celebrated the 42nd anniversary of the May 18th democratization movement. During its ceremonies, a pastor leading the celebration touted the great achievements of the Christian community in aiding in the democratization of South Korea. His depiction emerges from a long dominant historical narrative repeated by most contemporary Christians and even non-Christian Koreans alike. Yet, this paper will seek to complicate this narrative by viewing the Christian cause from the 1950s to the 1970s under the lens of anti-Communism. Beginning during the Rhee Syngman Era, this paper will transition into the Park Chung Hee era, taking into consideration the social, political, and cultural context of the time and how it influenced the Christian cause. This paper will argue that Christian Korean actors undertook varying positions on the issue of political liberalization and democratization, warranting a nuanced historical revision. Contrary to popular narrative, the Christian church, blinded by anti-communism, aided the dictatorial tendencies of Rhee Syngman and Park Chung Hee, only to later acknowledge their mistakes and participate in the democratization of the country.

The Historical Context of South Korea

The creation of South Korea

The end of Japanese rule ushered in a new era, one controlled by the people of Korea, but with independence came political strife. The Republic of Korea, a relatively small country, borders the lower half of a peninsula in the northeastern part of the continent of Asia. Bordering the Democratic People's Republic of Korea (North Korea), the Republic of Korea or South Korea is a "wholly modern entity" (Lim). From 1905 to the end of World War II in 1945, Korea had been under Japanese occupation, yet after the Allied victory in 1945, the winds shifted and rapid political change spread throughout Korea. Korea, once a whole nation, succumbed to international pressures that split it into two halves, the north and south, a decision made in extreme haste (Lim) The United States of America, the Soviet Union, and France had all agreed to put the nation of Korea under an international trusteeship, hoping to stabilize the nation before granting it independence. The Soviet Union took control of the area above the 38th parallel while the U.S. took control of the area in the south. Both the U.S. and Soviet states began swiftly building their respective regimes in the northern and southern spheres, neither willing to cede claims of legitimacy to lead the entire Korean nation (Lim). Thus, South Korea emerged on September 9th, 1948. The country, under American influence, claimed democratic leadership and assumed control under a presidential system. The country's first president, Syngman Rhee (1875-1965), gained sponsorship from the U.S., and his election was supervised by the American government; he held onto power until 1960 ("Syngman Rhee"). Although the legitimacy of the presidential elections appeared questionable under the supervisorial role played by the U.S., the country nevertheless undertook post-war rebuilding efforts and developed modern institutions commensurate with establishing the Korean nation on the regional and world stage.

Rhee Syngman

Many Koreans considered Rhee a patriot by all accounts during his early years. Born in Yi Sûng-man in P'yôngsan, Korea's Hwanghae Province, on March 26, 1875, Rhee went on to work furiously for Korean independence during the period of Japanese colonial occupation. As an editor for *Maeil Shinmun* (Daily News), he became increasingly drawn to *Independence Club*, an organization founded by Philip Jaisohn or So Chae-pi, with their own paper *The Independent* ("Syngman Rhee"). The club itself propagated Western-inspired political reformation. By 1898, the club disbanded due to rumors that they opposed the Japanese emperor. Authorities then arrested Rhee. He found Christianity in the dark walls of solitude. In August of 1904, Rhee regained his freedom and in 1905 December 31st, he reached U.S. soil with the intent of convincing the U.S. President to aid in Korean independence. After finding no success in the States, Rhee would find himself years later back in Korea on October 16, 1945, better known outside of his home country than inside it ("Syngman Rhee"). Here, after years of turbulence, Rhee found himself as the president of this young nation. However, his plans to lead this nation to greater heights would instead encounter hurdles along the way.

The Korean War

  His plans were quickly uprooted by another turbulence, the Korean War, which slowly eroded the democratic leadership in the South. On June 25th, 1950 North Korea invaded the southern half of the peninsula. Soon after, both the U.S. and a multitude of other countries engaged in fierce battles against the North Koreans and the Chinese who had come to militarily aid the North. Thus, it became so that the Korean War no longer was a battle between South Korea and North Korea, but a battle between the U.S. and its allies against "'international communism'" ("Korean War, 1950–1953"). After grueling battles, an armistice was signed between China, North Korea, the United Nations, and the United States at Panmunjom, putting an end to the fighting. In total, there were around one million casualties, including 152,000 dead, 383,000 wounded, 450,000 hospitalized, 21,300 POWs, and 4,000 missing in action on the Chinese side; 120,000 casualties for the North Koreans; 36,914 Americans killed; and 300,000 Korean soldiers and nearly one million more civilians killed for the South Koreans ("Korean War, 1950–1953").

  Such devastations created a shift in tone for the Rhee presidency. With his legitimacy eroding, he began to turn towards more dictatorial tendencies. Finally in 1960, after a blatant rigging of the presidential election, student-led protests drove him out of power. Rhee's resignation signaled the need for another system to choose the nation's leader. Thus, it was decided that a parliamentary system would instead be implemented, forming Korea's second republic led by two houses of the legislature that had the power to elect the president. However, the prime minister would be the leading political figure of the country under the new constitution instead of the president. Yet this second epoch of Korea was short-lived as Major General Park Chung Hee overthrew the newly appointed prime minister Chang Myon of the country's second republic in a military coup d'etat.

Park Chung Hee

  Despite shaping the Korean economy into one of the world's most powerful, Park served as a ruthless dictator neglecting human rights along with political progress. Park first established a Supreme Council for National Reconstruction or the National Assembly (SCNR), possessing both executive and legislative powers as well as assumed control. On May 16th, 1962, Park banned political dissent and established the KCIA under the guise of fighting communism, while using these powers to suppress, harass, and silence political opposition (Hamilton). Additionally, he had the Supreme Council rewrite the constitution, giving him readily available emergency powers and a stronger hold on the presidency. On October 15, 1963, Park won an election against Yun Posun, and on December 17 of that same year, he assumed the presidency, giving birth to the Third Republic of Korea. After winning his second term on May 3, 1967, Park took further steps to ensure his hold on the presidency; by September of 1969, the National Assembly revised the constitution once more, allowing Park to run for a third term. With a referendum by the public upholding the amendment, Park won his third term in 1971. While his third term brought him unprecedented powers, leading to many student protests, a national referendum in

1972 solidified his dictatorial stature ("Chung Hee Park"). The new constitution called the *Yushin Honpop* allowed for dictatorial measures to be taken by the Park administration. In 1975, Park issued a decree banning criticism against the government. In 1979, Kim Young Sam took a stand against Park and called out his dictatorship, sparking student-led protests that were quelled by the military. Finally, on October 26th, 1979, Park was assassinated by the head of the KCIA, Kim Kyu, bringing an end to his dictatorship ("Chung Hee Park").

History of Christianity in South Korea

Amidst this era of Korea's political evolution, religion and its prominent institutions appear irrelevant to this story. However, a detailed examination reveals the central role of Christian activists and leaders in shaping both the pro- and anti-government discourses and policies that ultimately resulted in long-lasting change. Furthermore, to understand this, we must first begin by discussing the relationship between Christianity and the Korean state in a deeper historical context. The first traces of Christianity on the Korean peninsula can be traced back to 1592 with Christian Japanese invaders (Kim 8) Yet it was not until the mid-18th century that Christianity truly came into contact with the Korean people. At first, many in the government opposed the foreign religion, believing it antithetical to the nation's Confucian root (Kim 10). No different was their persecution during Japanese colonial rule. Believing that Christianity went against traditional Japanese Shinto beliefs, the Japanese governors in Korea regularly imprisoned Christians (Kim 30). The winds began to change, however, after the liberation of South Korea from Japanese occupation. Christianity then took a more prominent role in politics and government. Christians first began to form a relationship with non-Christian and otherwise secular segments of society through "'people's committees,'" and some Christian leaders were even given governmental offices like Yo Un-hyung (Kim and Kim). Christians also founded political parties, such as the Christian Socialist Democratic Party (Kim and Kim). Additionally, during this period, Rhee Syngman returned from his exile in the U.S., where he had cultivated a substantial network of powerful Christian supporters that included the chaplain to the Senate, Frank Brown Harris. When Rhee returned to Korea, he was hailed as a patriot. Despite this, he did not have a base of support he could call his own in Korea (Kim and Kim). Thus he turned to the Protestants of the nation, becoming an elder in Chungdong Methodist church.

Christianity and Rhee Syngman

Rhee Syngman in advocacy for a Christian nation

To show his consolidation with the Christian cause, Rhee made advances in aligning government interests with those of the Christian church. At his inauguration, Rhee for the first time in Korean history took the oath of office while placing his hand on the Bible (Park 173). Additionally, he had Assemblyman Yi Yunyong, a Christian minister, lead a prayer of thanks which was equally unprecedented and not even on the printed program. Additionally, Christian members held great positions of power in Rhee's cabinet, with both the vice-president Ham Taeyong, and the acting prime minister, Yi Yunyon, as ministers of the church. The national

assembly also included church ministers and leaders such as Kim Sangdon, Hwang Songsu, Pak Yongch'ul, Kim Toyon, and Chong Ilhyong (Park 174). Additionally, it seemed to be the case that Christians although only 10 percent of the population constituted 40 percent of political leadership positions (Park 174). Under the watchful eye of Rhee, his governmental ministers inaugurated a "'Christian era'" in Korean politics (Park 174). Yet despite his works to uplift the Christian community, his political tendencies were less amiable. Rhee soon garnered the robe many strong men have in history, choosing a path of police and military might rather than peaceful political discourse to solidify his authority, setting a precedent for those who would follow. Yet as Rhee turned towards more dictatorial tendencies, his relationship with the Protestant community remained amiable, a fact often disregarded by many scholars and the general public (Park 174).

Christianity, Rhee, and anti-Communism

Such a relationship can mainly be understood under the lens of Christian anti-communist ideals. After the peninsula split in two and after the Korean War, persecution of Christians in the north proliferated. Such a development had impacts on the South and its Christian community. The tensions in the north between the government and Christians not only culminated in Rhee's favor but also established anti-communist ideals as a central tenant for contemporary Korean patriotism and helped solidify national identity (Park 176-178). This sentiment was perpetuated in light of the influx of refugees from the north who arrived in the south, many of whom either were already professed Christians or who converted after seeking shelter in the south. Therefore, the growing Korean Protestant community helped to legitimize his anti-communist government and state. In 1948, Rhee went on to give a speech to a conference of Presbyterian churches in the U.S., thanking them for bringing Christianity to Korea and stating that the biggest threat to his government and Korea was Soviet ideology, which aspired to wipe out Christianity in South Korea (Park 177). Afterward, Christian and government cooperation to rid communist ideology from the peninsula became even more intertwined by empowering the offices of the state to Christianize society as part of an overtly anti-communist social policy.

A prime example is the *Incident of the Christianity and Pro Communist Policy Pamphlet* (Kidokkyo wa yonggong chongchaek pampuretu sakon). The incident occurred in 1951 of Rhee's own volition, when he invited a group of Christian National Assemblymen to his temporary residence in Busan. There, he expressed his disappointment with the Korean National Council of Churches (KNCC) for not disassociating themselves with the World Council of Churches (WCC), which he believed to be too pro-communist, as they had not cut ties with churches in Eastern Europe. Additionally, he handed out a pamphlet in English that condemned the pro-communist tendencies of the WCC, which was later translated by fundamentalist pastor Song Sangsok, minister Yi Kyugap, and lay leader Hwang Songsu and sent out to the public. In response, the KNCC members fervently appealed their anti-communist stance, and by doing so, Rhee created a political reality in which Christianity and anti-communism were one (Park 178).

Political support of Rhee by the Christian community

Additionally, as they now shared common interests and sat on the same political aisle, Protestant Christian Churches mobilized their resources in support of Rhee, especially during election periods. In the 1952 presidential election, churches created the Korean Church Committee for Election (*Hanguk Kidokkyo son'go taechaek wiwonhoe*), which campaigned for Rhee and his affiliate party members. The church and the Korean Church Committee for Election made public statements in support of Rhee and his policies to install proper Christian values in their society. Furthermore, the church and its affiliated organizations were not simply limited to public statements. The Korean Church Committee for Election had a network of around 3,500 churches with 700,000 members, and before every election they would mobilize, printing newspapers and pamphlets detailing Rhee and his supporters and holding prayer sessions leading up to the final days of voting. Historically, unlike the political parties of the time, the Christian community had tremendous cultural, social, and even political power, which aided in Rhee's presidential campaigns. As such, Rhee now had the support of not only the military and the police but also the churches (Park 180).

Here, it can be seen that contrary to the dominant historical narrative, which underscores the social good Christian churches did during the Rhee era and the work done by them for democratization during the Park Chung Hee era, such a story tells a historical narrative that is often swept under the rug. Christian churches not only did not do anything to stop Rhee's dictatorial tendencies, but instead, they supported him, constituting a catalyst that brought him political success. Yet this non-dominant historical narrative surrounding Christian Churches is seen not only in the era of Rhee Syngman but also in the famed era of military dictator Park Chung Hee.

Christianity and Park Chung Hee

Christian support of Park's newly formed regime

The Protestants welcomed the May 16th Coup and Park Chung Hee with open arms, believing Rhee to have strayed away from his anti-communist roots during the latter half of his regime. The KNCC issued a statement of support immediately after the coup, highlighting how Park would bring about a change, rescuing the nation from Communist aggression. In July 1961, Protestant intellectual Hyon Yonghak made a more reserved claim in an issue of *Christian Thought*, supporting Park's regime as long as he kept his promise to the Korean people. His support, however, stemmed from a hope that Park would further the anti-communist agenda. After the 16 May Coup, Protestants adopted a new idea, "'Poverty is a sin, and we must get out of it to defeat communism'" (Yoon 252). The Catholic viewpoint aligned in many ways, except for their preference to remain distant from staunchly anti-communist social crusading, preferring instead to promote the containment of communism. Here once more, it can be seen that the support of churches in dictatorial regimes under the guise of fighting communism. Contemporary scholars of the Koran church in this era especially tout the social good the Christian community

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did. While this is not unfactual, their tendency to disregard the workings of the majority that ultimately upheld dictatorial powers and authoritarian regimes remains underappreciated.

Christians against the Park regime

Yet at the same time, while it is undoubtedly true that the majority of the churches remained idle or even supported the Park regime during its early stages, a force of churches also fought against the regime given that he had no intention of relinquishing his grip over the state. Although these tales of a progressive Christian church against the Park regime have become the only historical narrative in the eyes of contemporary Christians, their merits must also be appreciated. The Christian church's role in democratization first started around 1970, when it became apparent that Park had no intention of leaving office even after he had served the constitutionally mandated term limit of two terms (Yun-Shik 438). The Korean Student Christian Federation and young progressive Protestant ministers initiated the opposition, the National Council of Churches of Korea (NCCK), representing one-third of the Christian population, who joined not long after in 1972 when Park adopted the Yushin Constitution (Yun-Shik 438). Branding the Yushin Constitution as "'an evil force destroying constitutional democracy and undermining basic human rights and dignity,'" the NCCK pushed for the abolition of the Yushin Constitution and Park's dictatorship. The Catholics shared a similar view with the Catholic churches voicing their disapproval of the dictatorship as well. Additionally, many Protestant leaders began to reflect on their complacency during the Rhee regime, revoking their support of Rhee and his dictatorial tendencies (Yun-Shik 440). Younger leaders in the church especially took a more apologetic stance, urging the elders to cease hosting prayer sessions for high-ranking government officials.

The ministers and church members also took more active measures outside the bounds of the church. For example, in 1967, church leaders collected one million signatures to demand the revision of the constitution, boycotted the referendum for the Yushin constitution, and formed a ballot inspection group in the thirteenth national presidential election. Furthermore, in 1974, the NCCK established the Human Rights Committee, providing legal assistance to families persecuted unjustly by the government and sending financial assistance to those who had been incarcerated unfairly (Yun-Shik 446). Furthermore, the Protestants established the Urban Industrial Mission (UMI) while the Catholics established their counterpart to the UMI, the Catholic Youth Labor Organization (JOC). These two organizations worked to educate workers on their rights, aid in labor disputes, and provide shelter and food to expelled factory workers (Yun-Shik 451). Various extensions of the labor movement, such as the Capitol Area Mission Committee (CAMC), advocated for the urban poor focusing on property disputes, and the Catholic Farmers Association (CFA) focused more on the rural areas of industry and advocating for farmers (Yun-Shik 452-453).

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Conclusion

      Social good done by the church to work for freedom and democracy must undoubtedly be remembered. At the same time, non-dominant historical perspectives complicate these celebratory depictions, which help form a nuanced awareness of Korea's political history. This requires investigating bodies of evidence that do not simply fit into a celebratory narrative. In order to accomplish this goal, religion must not be studied in a vacuum. Instead, it must be viewed as a sociological construct, taking evidence and analysis from not just a religious perspective but a historical and even sociological one. As seen above, religion is deeply intertwined with politics and culture, and its historical trends are complicated and nuanced, possessing many narratives that often contradict the hegemonic narrative pushed by many individuals. However, by utilizing a diversity of sources and integrating multiple political and religious actors into this history, a better understanding of Korea's religiosity is achieved, one that is not only more accurate but attuned to variations from normative positions. The complication of the Korean churches' participation in democratization is one that is not uniform to a historical narrative or field of study. Thus, it does an injustice to the public historical consciousness to view Christian work during the 1950s-1970s as an isolated incident and instead should be viewed in tandem with the cultural and political structure of the state and society during this era.

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Understanding Geoengineering and How it Can Combat Climate Change By Alisha Ahamed

Abstract

Geoengineering is a concept that refers to the deliberate modification of the planet to slow down rising temperatures. It consists of several different schemes including solar radiation management and marine cloud brightening. While climate change is a serious topic that requires immediate action, geo-engineering methods can result in acid rain, harm entire ecosystems, and develop many more detrimental effects. There are also several ethical issues surrounding geoengineering from the impact it will have on countries uninvolved with the technology to how politicians may take advantage of the concept to avoid stopping climate change. Overall, it may sound like an effective solution to global warming but is actually an unpredictable idea that is in need of a lot more research before it can be implemented in today's world.

What is climate change?

Climate change is the alteration of Earth's environments and weather conditions over long periods of time. There are several different natural forms of climate change seen on our planet that are known to occur over hundreds to thousands of years. By the end of the 1980s however, the natural transformations of Earth's weather began to see drastic changes for the worse and began causing detrimental effects on our planet as a result of humans' heavy usage of fossil fuels along with other damaging factors. This form of climate change also happens to be the most widespread and alarming, coining the familiar new nickname; global warming. Global warming is a term used to describe the planet's rapidly increasing temperature. Unfortunately, if measures are not taken to prevent it, global warming may transform Earth into an uninhabitable planet, by making it too hot to live, drowning parts of continents as a result of melted glaciers, damaging several ecosystems, and much more. The solution to solving climate change is not an easy one. The main causes of the changing of the Earth's atmosphere and environments are results of the 21st century's industrialized world. From day to day transportation, the manufacturing of goods, and power generation, it is easy to conclude that climate change today is fueled by processes that humans heavily rely on. Now you may be thinking, if global warming was caused by such activities, why is it emerging itself as a problem only now, when fossil fuels have already been normalized for nearly 150 years?

Not Acting Quick Enough and Need for Alternative Cooling Solutions

Global warming roughly began in the late 19th century as a result of the emergence of the industrialized world. The United States coal consumption from 1966 compared to present day has doubled from 2,500 tWh of coal and to a present day value of 5,000 tWh[42]. With technological advancements increasing our reliance on non-renewable waste and the overall

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[42] ourworldindata.org

increase of our planet's population, fossil fuels have naturally been consumed more over time. Other than Earth's shocking increases in temperature, we need to also learn to deal with other forms of climate change, including rise in sea levels and the melting of glaciers. These factors, along with many more, have put humans and other animals' lives at risk, greatly demonstrating the need for a solution to climate change. Because we have failed to act quick enough, climate change has only brought about more problems and has already caused irreversible damage that only continues to puts us in danger. Our reluctance to recognize global warming and other forms of climate change as actual life threatening problems has only made coming up with a solution even harder. To come up with a solution for climate change, we must go back to its root and main cause, which is the use of fossil fuels. This is a difficult situation because humans have a huge reliance on fossil fuels and use it for day to day tasks including: transportation, manufacturing, and electricity. Since ending our consumption of fossil fuels has proven to be a difficult task, many scientists sought out to find alternative methods or forms of renewable energy to cool our planet and slow down climate change. Because climate change is a growing and imminent problem that will affect all of Earth's inhabitants, developing a method to slow it down is critical if we want to have a planet to live on in the future. Geoengineering comes into play here because while actual solutions are in the making, this technology may be able to slow down climate change and give scientists the extra time that they need.

What is geoengineering?

Geoengineering is a concept that refers to the deliberate modification of the entire planet to slow down climate change. For something to be classified as geoengineering, the results must be large scale and the alteration of the planet should be the goal, not a side effect[43]. Its main purpose should not be just 'grand', but instead to also create a method to combat climate change. Ever since its creation however, geoengineering has been a controversial topic. This is because the entire idea behind geoengineering, altering our planet on a global scale, is incredibly dangerous, unpredictable, and to many, viewed as unethical. As of right now, our planet desperately needs a solution and geoengineering might be the closest thing we have to one. This form of technology can potentially slow down the planet's increasing temperatures and present itself as a solution to the global warming crisis if scientists gave it a chance and invested their time and money into it. To do this, they would have to experiment and test several geoengineering schemes to see if they are effective in combating Earth's dangerously high temperatures and growing signs of climate change. Some schemes include stratospheric aerosol injection, marine cloud brightening, and ocean fertilization. These procedures could hypothetically slow down increasing temperatures on our planet and buy scientists actual time to come up with a real solution.

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[43] GEOENGINEERING THE CLIMATE: History and Prospect

What is a geoengineering scheme?

As explained before, geoengineering schemes are defined by having fulfilled two goals. Their execution must somehow affect the planet on a global scale and succeed in mitigating the many different effects of climate change. An example of combating climate change could be either removing carbon dioxide from the atmosphere, specifically known as carbon dioxide removal, or reducing the amount of sunlight that even enters into our atmosphere, better known as solar radiation management (SRM). Both of these concepts are the basis and foundation of the many geoengineering schemes known today. The geoengineering schemes to be mentioned are only a few of the many that exist. Their procedures are only the most well known or most likely to be conducted in the near future.

Stratospheric Aerosol Injection

The most commonly discussed and well known geoengineering method is stratospheric aerosol injection. This scheme falls under the solar radiation management umbrella because the entire concept revolves around reducing the amount of sunlight that enters Earth's atmosphere. The idea behind this scheme is that by injecting sulfur dioxide particles into the Earth's albedo, or the portion of the atmosphere that reflects sunlight rays that enter it, it will deflect more sunlight. By sending back even more of the rays of sunlight that enter our atmosphere, this process can decrease the temperature of our planet and cool it down to the point where global warming slows. Stratospheric aerosol injection is inspired by volcanic eruptions, which naturally release tons of sulfur particles into our atmosphere and deflect the sun's rays. While this scheme would be the deliberate work of scientists, there have been records of coal plants releasing sulfur dioxide into the air and producing similar results to what solar radiation management would do.[44] This scheme, which was first discussed in the 1990s unfortunately has little to no research into making it a reality.[45]

Sunshades in Space

The sunshades in space geoengineering scheme, also a method of solar radiation management, revolves around the idea of a football field sized sunshade being sent into space to orbit around the planet. Its goal should be to reflect any sunlight that hits it in order to prevent rays from entering Earth's atmosphere.[46] If it manages to deflect large amounts of solar radiation, this geoengineering scheme can lower the planet's temperature, possibly becoming another solution to the planet's warming problem. While this geoengineering scheme does seem to have lots of potential in helping our planet, not enough research or experimentation has gone into figuring out whether or not this could even be possible or how to implement it into our world.

Marine Cloud Brightening

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[44] Ranking geo-engineering schemes
[45] Ranking geo-engineering schemes
[46] The solar shield concept: Current status and future possibilities

Marine cloud brightening is a procedure that consists of spraying sea water from large ships in the middle of the ocean that will make the clouds whiter.[47] The brightening of the clouds will then allow the sun rays that enter our atmosphere to bounce off the white clouds and consequently prevent our planet's temperature from increasing. Unlike the previously discussed geoengineering schemes, this method is not a direct way of deflecting the sun's radiation and solar rays. This geoengineering scheme was only brought about more recently and like the rest of the schemes is yet to have research conducted on it.

Ocean Fertilization.

The last geoengineering scheme is ocean fertilization. Unlike all the schemes mentioned before, ocean fertilization is not a form of solar radiation management but instead a method that involves carbon dioxide removal. In this process, the ocean environment is manipulated and altered so that there is an increase in phytoplankton activity.[48] These microorganisms are able to collect carbon dioxide that enters the bodies of water that they're in. An increase in phytoplankton population accordingly also increases the amount of carbon dioxide being taken in. This geoengineering scheme can theoretically decrease the amount of carbon dioxide in our atmosphere. Of the research that has been done on this method, scientists were able to conclude that if ever carried out, ocean fertilization could mess up the delicate relationship in an ocean environment between all the living organisms and also negatively affect the populations of certain aquatic animals.

The Technical Problems with Geoengineering

While all the geoengineering schemes listed above likely have the potential to help cool our planet itself as a solution to the increasing climate change Earth is facing, from the very little research conducted, scientists have been able to conclude that along with the solutions that they are supposed to create, there are many problems as well.

The first problem with geoengineering is that most of its schemes result in negative effects on our environment Although a geoengineering scheme might be successful in mitigating climate change whether by preventing how much sun enters our atmosphere or how much carbon dioxide is released into the air, it can greatly alter our climate in ways that are not suitable for human life. For example, the geoengineering scheme stratospheric aerosol injection, where sulfur dioxide particles are released into the atmosphere to reflect more sunlight when rays enter the planet, can result in heavy acid rain.

Another consequence of geoengineering to be aware of is that most of its schemes could potentially damage and change Earth's hydrological cycle aside from causing acid rain. This means that certain geoengineering schemes can affect how much or how little rain certain parts of the planet will receive. For instance, some parts of the planet may go into drought while others will undergo heavy monsoons. Specifically, in a study conducted by Nature on climate change,

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[47] Ranking geo-engineering schemes
[48] Science Background – Ocean Fertilization

the countries India and China will experience immensely heavy floods and monsoons if stratospheric aerosol injection was to be implemented in our atmosphere.[49] This is yet another problem with geoengineering because water is essential and the most important resource to all living creatures. Changes in accessing water could and will create huge problems for the millions of animals on Earth.

Another problem that exists within the ocean fertilization geoengineering scheme are the changes that underwater ecosystems will undergo when the number phytoplankton is increased to sequester carbon dioxide deep underwater.[50] Without proper research and study, the thousands of fragile ecosystems the ocean contains can be easily damaged if something as large as increasing the population of a certain species occurs. Because the many ecosystems are closely interrelated and connected to each other, a small change in one can result in large changes in the others.[51] From creating acid rain, droughts, monsoons, and causing huge changes in certain oceanic animal populations, geoengineering, if ever put into action, will inevitably result in drastic changes in our environments and their inhabitants.

Little experimentation has gone into putting geoengineering schemes in action. It's also important to keep in mind that geoengineering by itself is not one sure or complete solution to climate change. This unfortunately makes government officials reluctant to spend so much money on something that in the end is not truly a solution. Many actually don't find it worth investing money and time into something that could possibly save our planet but could also create so many other problems. Another issue with this is that politicians may use geoengineering as an excuse to avoid moving away from fossil fuel consumption. A huge reason as to why geoengineering is needed in the first place is our planet's heavy dependence on fossil fuels. We as a society rely on them for common tasks, and as a result our daily lives end up contributing largely towards climate change. Geoengineering would be one of many methods to save our planet but not ever truly be the sole solution. Politicians taking advantage of geoengineering would become a huge problem if they actually did because it would mean that an actual solution is not being developed.

Unknowns

Lastly, the biggest problem with geoengineering overall is that it contains many unknowns. Not much research has been put into studying these proposals for scientists to be able to confidently conclude that they are safe to perform. Many argue that scientists will never truly know if a geoengineering scheme is successful until actually performed. The problem with this however is that the entire technology as a whole cannot be experimented or tested with because it can affect the entire planet. To be able to help our planet, scientists need to do the research and study more about geoengineering even if it is just to rule out the possibility of it ever being some sort of method to mitigate climate change.

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[49] Stratospheric aerosol particles and solar-radiation management
[50] Ranking geo-engineering schemes
[51] Geo-engineering might cause, not cure, problems

Should We Really Alter Our Planet on a Global Scale?

The biggest ethical concern with geoengineering is whether or not we should even tamper with the delicate ecosystems of our planet in the first place. When considering this, it's not really a matter of 'is it possible?', but instead 'should this even be conducted?'. When discussing the topic of geoengineering, scientists constantly debate whether or not it's even worth putting in and investing money into researching geoengineering. The main concern now is will geoengineering hurt our planet even more. The scientific community constantly debates whether or not they should tamper with something they cannot bring back. Many people feel that humans should not destroy what they cannot create. This brings us to the question, if we've already messed with the planet so much already, why not experiment with it some more?

With geoengineering, something to keep in mind is that the entire process affects the entire planet even if other parts of the world did not want to take part in the experiment. To elaborate, if for example the United States decides to conduct an experiment involving stratospheric aerosol injection in certain states, positive results may occur in the U.S. All across the country, temperatures would theoretically decrease, counteracting climate change and global warming. However, other countries like India or China who saw geoengineering as unsafe and chose not to participate in this process may experience side effects as a result of experiments occuring in the United States. The countries of India and China may experience monsoons that affect their economy, population, and overall way of living even though they didn't participate in geoengineering[52]. Even if an experiment is done in one country, geoengineering side effects and consequences can possibly be seen in another. Whole entire countries who choose not to get involved with geoengineering may have to pay for the actions of other people. If the state of the planet was to ever get so bad that these decisions had to actually be made, people would have to come to an agreement on how they would be decided. Whether or not the vote would be based on majority or unanimity is yet another decision that would have to be made, proving that there are countless factors to consider when thinking about geoengineering even if just discussing its ethics.

My Thoughts

We can conclude that there are not many steps being taken to implement geoengineering in today's society because there isn't enough research done on it to draw enough inferences as to whether it's safe or if they will work. Such a grand experiment on our planet cannot be taken lightly and must have several precautions taken to make sure that no one is harmed all while coming up with an actual solution to our never ending climate crisis. At the same time however, even if geoengineering has lots of problems we still need to know more about them even if it's just to eliminate one geoengineering scheme. Geoengineering only slows down climate change and it alone is not a true solution. The second geoengineering is stopped, climate change and the several problems that come along with it will only continue to create problems for the planet, and unfortunately for us, at an even faster rate. I believe that if research is being put into studying

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[52] Stratospheric aerosol particles and solar-radiation management

geoengineering that doesn't mean that there shouldn't also be people studying actual solutions to climate change as well. Both must be done at the same time, and fast, if we want to have the possibility of saving our planet. As also mentioned before, when it comes to the most realistic geoengineering scheme, also known as solar radiation management, the biggest concern is that if carried out on our planet, there are negative side effects that scientists have discovered and identified as acid rain. Because this geoengineering scheme has not actually been used, there could still be unknown side effects that scientists are unaware of due to the lack of research. However, some research has been conducted by scientists on other chemicals to inject into our atmosphere instead of sulfur particles could possibly create the same results. This could potentially allow Earth's albedo to reflect more sunlight but without the harmful side effects like acid rain. The research done on the feasible substitutes for sulfur dioxide particles only proves that despite being such a risky and taboo concept, with enough research and experimentation, even the flaws and challenges that geoengineering presents can be overcome.

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Exploring shared neurobiological mechanisms across Bipolar Disorder, schizophrenia, and Autism Spectrum Disorder By Amani Multani

Abstract

Within the mysterious world of the human body, symptoms transcend the normal physical boundaries of several diseases: hypersensitivity, mania, and psychosis. For example, patients with hypersensitivity need to address triggers to adapt to the world comfortably. Similar stages in the development of disorders often arise in bipolar disorder (BD), schizophrenia, and autism spectrum disorder (ASD). All three conditions are highly associated with genetic factors, neurotransmitter imbalances, altered brain structures, and environmental stimuli. Although these conditions share many of the same symptoms and are associated with many of the same possible causes, it is unclear why these diseases share symptoms and how their mechanisms may be interrelated. This review will examine risk factors for development of these disorders and improve our understanding of comorbidity across these disorders about these three diseases.

Introduction

Bipolar Disorder (BD), schizophrenia, Autism Spectrum Disorder (ASD) all share symptoms and similar underlying disruptions in genetics and brain morphology.

Bipolar Disorder is a progressive, mental health disorder associated with emotional phases of "highs and lows", often shown in heightened behaviors (26). It has symptoms ranging from mania to depressive states which show up in episodes throughout the disease. There have been several treatments such as mood stabilizers (27) that have been effective to manage the severity of symptoms to counteract manic highs. Aside from medication, there are therapies such as Cognitive Behavioral Therapy (27) which identifies behavior and works individuals through identifying problems and reactions (28).

Schizophrenia is a chronic lifelong brain disorder that can alter one's perception of the external environment, produce a loss of touch with reality, and change behavior and decision-making (29). There are two main symptom types (positive and negative) that vary and are shown episodically throughout the onset of the disorder (21). Positive symptoms, usually shown as "excess" from normal behaviors, are found in symptoms such as hallucinations and delusions (30). Negative symptoms are less stimulating and instead produce more withdrawn behavior. Usually negative symptoms can be seen in bleak emotional responses and less coherent speech (31). Common treatments for schizophrenia are psychosocial intervention and antipsychotic drugs (32) which address the severity of symptoms and aim to reduce this.

ASD is a neurodevelopmental disorder that can be detected with early signs shown during childhood (18). Individuals with ASD miss out on certain age milestones such as talking or communicating, instead hitting these milestones much later than normal. Over time, as the child develops, social challenges may arise and interactions with the surrounding world may be difficult due to symptoms like hypersensitivity. Individuals with ASD cope with the world

through repetitive behaviors. Current treatment is cognitive behavioral therapy; however, understanding the underlying cause of this disorder may create more targeted treatments.

Overlapping symptoms in BD, schizophrenia, and ASD can be accredited to a combination of genetic dispositions, dysfunctional sensory processing regions, the prefrontal cortex, and environmental factors. Manic symptoms include elevated moods and energy. Psychosis is characterized by delusions and hallucinations. The mesolimbic system and amygdala in the brain drive both mania and psychosis. The Prefrontal and hippocampal regions are different between the disorders. Hypersensitivity impairs the ability to process stimuli. Collectively, all these symptoms can impair the wider cognitive functioning in patients. Studying the shared regions may allow us to understand why psychosis and mania may present similarly at times, while studying the regions that are not shared may give us insight into how the underlying disorders differ.

In BD, individuals may experience a mild manic state for prolonged periods of time which may lead to a manic episode. Manic states are characterized by heightened emotions and behaviors that stay over prolonged periods of time. Other manifestations of BD can lead to hypersensitivity to emotions, cognition, and the environment during these periods. ASD also shows hypersensitivity with environmental stimuli, which may produce heightened emotional responses. Some ASD patients have developed all three disorders as a result of mutations in genes such as Neurexin-1 (*NRXN1)*, which encodes for a presynaptic protein (20). NRXN1 has been linked to presynaptic and postsynaptic neural connections in the brain and is significant to brain connectivity on a neurobiological level (20). Mutations in *NRXN1* are actually a risk factor for all three disorders, likely due to the protein's importance in establishing proper connections in the brain.

Moreover, through gray matter structural magnetic resonance imaging (MRI), used to study brain activity, imaging showed gray matter reductions in the cortical and subcortical gray matter regions of BD and schizophrenia (14), playing more into the dysconnectivity that plays into the development of symptom severity. Through such research, researchers can implicate more earlier methods of detection and begin to look deeper into advancing an understanding of brain disorders like BD, ASD, and schizophrenia. This paper aims to explore the shared neurobiological and genetic etiology of BD, schizophrenia, and ASD by investigating overlapping symptoms, brain structural abnormalities, and genetic factors.

Discussion:
Symptoms and progression of BD, schizophrenia and ASD

Based on BD's development, symptoms are progressive and can vary in severity. Alongside this, brain regions show different propensities for dysfunction amongst all three disorders. The manifestation of shared symptoms across a spectrum of mental health disorders, with varying courses of progression, is caused by shared underlying neurobiological and genetic factors.

BD is a mental illness that progresses and is characterized by emotional "highs and lows" as well as elevated behaviors. It progresses through a variety of stages, beginning with the prodromal stage. (1) In this stage, changes in behavior and emotions before the episode begin to show. It progresses into an acute state where manic episodes and major depressive episodes usually cause social and societal impairment (3). This slowly starts with one manic episode and progresses into more cyclic episodes within individuals (3). Usually, after the manic episode, depressive episodes occur, producing what can be a mixed mood state with a combination of manic and depressive moods (7). After the onset of the disorder, there is a maintenance stage where BD individuals may begin the management of their disorder for more functional behaviors with the use of medication and therapies.

BD and schizophrenia show commonalities in the dysfunction of similar mechanisms in the mesolimbic system and amygdala. Specifically, the manic and hyperactive stages are similar between both disorders. These similar symptoms are likely associated with the same brain region.

Schizophrenia is a lifelong brain condition that can cause changes in behavior and decision-making, as well as a loss of reality and perception of the outside world (1). Before psychotic symptoms, there are changes in cognition and behavior that usually show in the prodromal stage, similar to BD. Usually, 73% of people experience prodromal symptoms such as depression and irritability before the onset of the disorder (2). This underscores the onset of illness and how, overtime, episodes become more predictive as symptoms become cyclic.

Individuals with ASD may be at a higher risk of developing psychotic symptoms such as those found in individuals with schizophrenia and BD. ASD is a neurodevelopmental disorder that can be detected by early signs shown during childhood, mostly up until 18 months (18). Individuals with ASD miss out on certain age milestones such as talking or communicating, instead hitting these milestones much later than normal. This is different from BD and schizophrenia which only become apparent later in life.

During the Early Developmental stage, interactions with the outside world may be shown through disinterest at around 9 months of age along with delayed reactions to the environment (1). As the child develops, social challenges may arise and present a period of difficulty in interaction and recognizing social cues around them, similar to the withdrawal seen in schizophrenic individuals. Repetitive behaviors such as stimming are associated with ASD and can come off as coping mechanisms individuals use to seek comfort throughout the progression of the disorder. As children reach the adolescent stage, further challenges continue to arise.

According to the DSM-5 manual, there are three levels of ASD (1). Level 1 individuals need support and may have mild and hard communication with peers and in response to social cues. Level 2 individuals need substantial support with symptoms such as losses in verbal and social communication arising. Individuals cannot focus as much and may present narrow behaviors tied to interests. Lastly, Level 3 individuals require the most substantial support. They present as the most severe on the spectrum, and show the same behaviors as Levels 1 and 2, however to function, they must be in a familiar environment (1). An interesting area of research

would be to understand if individuals with certain levels have a higher risk of developing other conditions like seizures. Level 3 individuals may have a higher risk of developing more psychotic symptoms due to how the brain may be less functional, thus increasing the susceptibility to these psychotic symptoms.

Overview of Mania and Psychosis in Disease

Mania and psychosis are both distinct hallmarks of mood and psychotic disorders. Dopamine is a neurotransmitter that plays a role in the pattern of these behaviors. To understand why psychosis and mania are prevalent in these disorders, it is useful to understand how these symptoms manifest and develop. Mania is defined as a period of at least one week where a person changes normal behavior that can significantly affect functioning (6). Symptoms range from elevated moods to the progression of psychotic features such as delusions and hallucinations (7). On the other hand, psychosis is defined as a combination of psychological symptoms which can result in a loss of touch with reality (5), which is a common symptom in many psychotic disorders such as schizophrenia, and is closely linked to the dopamine pathway.

Characterized by a state of highly elevated mood changes and excessive overactivity, mania often manifests in phases and can heighten with irritants such as overstimulating environments, leading to worsened manic symptoms. Psychosis refers to a disillusioned condition where perception of the world is indistinguishable from reality. Symptoms such as auditory hallucinations from breaks in reality psychosis arise in schizophrenia. Similarly, hypersensitivity, states of heightened emotional responses to "normal" behaviors, amplify with reactions to stimuli and is commonly found in individuals with ASD.

Positive symptoms, symptoms that alter behaviors and emotions (21), are commonly found in schizophrenia and may show through changes in behaviors and moods, through symptoms like delusions and hallucinations. These symptoms have been linked closely to the dopamine pathway, specifically from excess dopamine in the mesolimbic region, which controls cognition (6). Cognition in the mesolimbic system allows for an accurate perception of the environment; however, when dysfunctional, it may lead to inaccurate views of surroundings and perceptual abnormalities (6). Through this excess in dopamine, hyperactivity in the mesolimbic region can lead to a signaling imbalance which can progress into positive symptoms (8).

Delusions (a positive symptom), another hallmark of psychotic disorders, are defined as false beliefs without evidence to prove truthfulness (12). In schizophrenia, they are commonly persecutory (illy intended) delusions with many patients thinking others are out to get them. Hallucinations (another positive symptom) are defined as experiences sparked without an environment and may be present in vocal and tactile ways. As opposed to positive symptoms, negative symptoms are usually presented through withdrawal from the outer world and disinterest in normal activities, which may lead to losses in normal function through symptoms like bleaker emotions and poor speech. With varying levels of dopamine regulation, different symptoms transpire, as normal threshold levels are imbalanced.

Goldberg's Theory of psychosis characterizes symptoms as levels which follow a hierarchical model. Each level is responsible for proper functioning, however if one becomes dysfunctional it contributes to the progression of the symptom. Based on Goldberg's theory, psychosis presents a hierarchical model. Starting from the bottom, the model begins with the input of stimuli, and goes to higher levels which interpret these stimuli (25). Symptoms may manifest simultaneously. This is hypothesized to be due to dysfunction at one level of hierarchy which trickles upwards or downwards to other levels (25). Hallucinations come from dysfunctional lower levels of hierarchy, which are responsible for the basic features of stimuli, while delusions present from higher levels of dysfunction in cognition based on the integration of these stimuli (25). Within the hierarchy, the mesolimbic region may present through higher-level dysfunction, which raises the question of what causes lower-level dysfunctions in the hierarchy. An answer might emerge from examining the brain areas that underlie the different disorders.
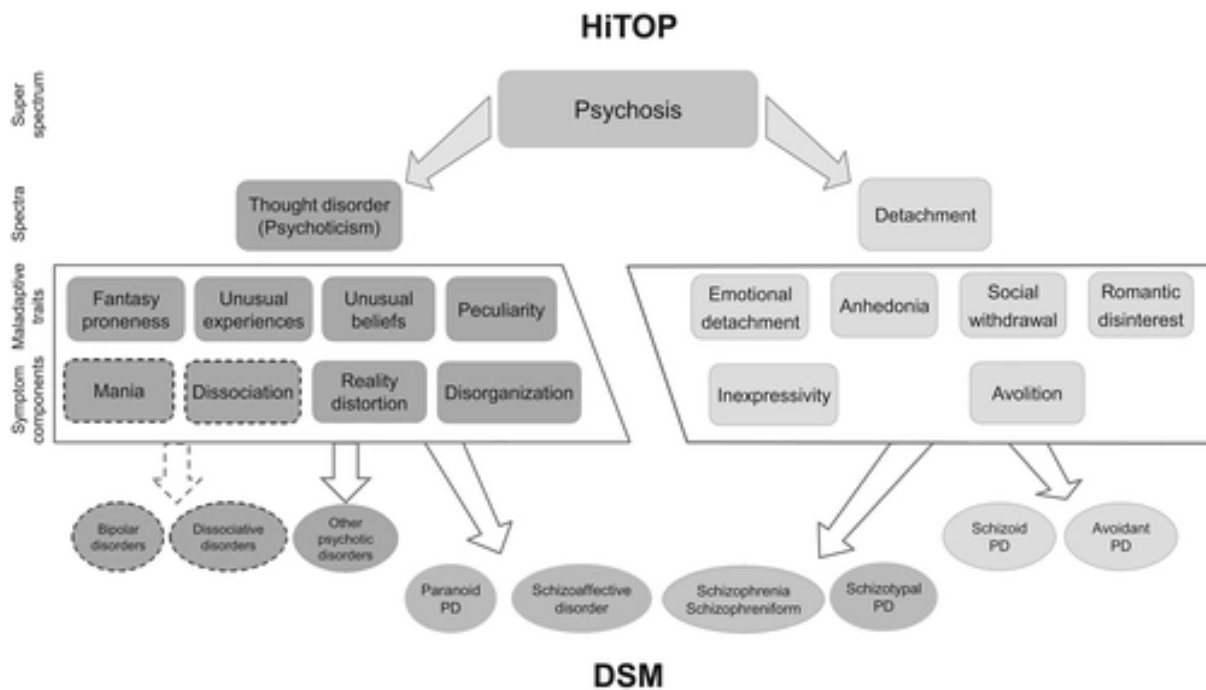
Figure 1: This image illustrates the hierarchical structure of psychosis, as proposed by Goldberg. It shows the organizational nature of symptoms, and how all three disorders are mutualistic (33).

Brain regions associated with BD, schizophrenia, and ASD

Mania has been associated with the amygdala and its hyperactivity, whereas psychosis has been linked to reduced gray matter throughout several regions of the brain (16). This raises the question of how these specific abnormalities can lead to such drastic effects. Findings discovered through MRI via neural timescales show how long information is integrated into specific brain regions. Neural timescales in the lower levels of the hierarchy were usually longer in patients with more severe hallucinations which could lead to more hypersensitivity to stimuli and perception, whereas neural timescales in the higher levels were longer in patients with more

severe delusions (14) suggesting more dysfunctional cognition. These underpinnings prove how the lower level, which is more responsive to external stimuli, can progress into more hypersensitivity to stimuli.

Patients with BD show characteristics of a hyperactive amygdala and a hypoactive hippocampus and prefrontal cortex. With higher activity in the amygdala to process stimuli along and decreased activity in cortical regions, this could lead to impaired executive function, impairing cognitive skills to plan and accomplish goals. Through mania, emotions are heightened and uncontrollable (7). By measuring cortical activities, research indicates that reduced gray matter in the prefrontal, superior, and medial temporal regions of the brain is common amongst people in their first episodes of BD. Overall, the thalamic and amygdalar dysconnectivity responsible for sensory processing and increased connectivity to the mesolimbic regions show the progression of abnormal neural circuitry which may lead to the comorbid development of psychotic symptoms.

Reasons for Shared Symptoms (Hypomania, Sensitivity, Psychosis) across Diseases

Through the psychosis spectrum, reduced brain connectivity is present in some regions, however there is increased connectivity in the mesolimbic areas, most responsible for emotional regulation (22). Overall, it is hypothesized that such brain connectivity may lead to emotional dysregulation which could occur in response to heightened emotional symptoms within BD. In schizophrenia, decreased connectivity in sensory-motor and mesolimbic areas are shown to lead to the improper processing of surroundings and impaired motor skills attributing to the loss of experiences in spatial perception. Moreover, through the mesolimbic connection to the dopamine pathway, dysfunctional circuits and dopamine imbalance may then progress more into negative symptoms associated with schizophrenia such as disinterest in once pleasurable activities (6).

Through new knowledge of the integration of emotions in dysfunctional brain regions associated with BD, schizophrenia, and ASD, more targeted treatments can be implemented that are associated with emotional regulation problems. Gray matter structural magnetic resonance imaging in the cortical and subcortical gray matter regions has been informative in understanding how brain region volumes vary across disorders. (14). Compared to BD there is more volume loss in schizophrenia, and these decreases in volume typically involve the hippocampus, thalamus, and amygdala (34). Though both are episodic disorders, there were more abnormalities in the cortical and subcortical volume within schizophrenia individuals (35). Schizophrenia shows how with more loss in gray matter volume comes a larger and more severe first episode of schizophrenic symptoms. This volume loss signifies how such structural abnormalities can relate to the severity and frequency of psychotic symptoms in an episodic manner

Gray matter structural MRI also showed abnormalities within white matter which can be found more deeply in the subcortical tissue and is responsible for nerve signaling (36). Psychotic BD patients showed more diverse white matter loss compared to schizophrenic patients who showed Fractional anisotropy (FA), a method used to measure diffusion in water matter lobes, reduction in the temporal and occipital lobes (14), showing less connectivity to perception and

physical perception of the outside world. Alongside this, reward anticipation in the ventral striatum decreased in schizophrenia patients but not in manic BD patients. This could tie back to an imbalance of dopamine levels (responsible for reward signaling) in the mesolimbic circuitry thus producing more bleak emotions and displeasure in once pleasurable activities. With more striatal dopamine dysfunction, it may lead to anhedonia (37).

Through the resting state functional MRI, a different MRI technique, researchers measure low-frequency waves to signal activity at the resting state, and any brain connections (14). This measurement can help researchers understand how changes in certain brain regions could cause symptoms in diseases. On example is that in patients with schizophrenia there was is In the resting state, medicated schizophrenic patients showed decreased activity in the medial prefrontal cortex, left hippocampus, posterior cingulate cortex, and precuneus, all of which play into the default mode network (14). This network primarily controls verbal and visual memories, internal thought, and memory (23). The MRI also showed increased activity in the lingual gyrus, accredited to high visual processing that may be found in visual hallucinations. BD and schizophrenia patients showed a shared reduction in the default mode network connectivity to the hippocampus and fusiform gyrus (38), which could accredit to a dysfunctional high-level perception that may be found within hallucinations. Increased connectivity with the primary visual cortex, could help explain more into the progression of hallucinations seen in the disease. If the primary visual cortex is dysfunctional, a mix of misinterpretation of visual input and high-level perception are correlated with visual hallucinations.

In some cases MRI studies can help us identify brain regions that are similarly affected in different disorders. For example, connectivity within the mesolimbic areas also varies amongst BD and schizophrenia. In BD, resting state functional MRIs show increased connectivity in frontotemporal and mesolimbic areas (14). Such connectivity can increase hyperactive behaviors ranging from mood swings from dopamine imbalances to impulsivity and heightened behaviors (14) . Schizophrenia shows decreased connectivity in sensory-motor and mesolimbic areas which may alter the ability to integrate stimuli-based responses and more anhedonia-like emotions (8). However, BD and schizophrenia share thalamic and amygdalar dysconnectivity, and patients show no difference in hippocampal connectivity (14). Such dysconnectivity could alter sensory information processing along with more issues in emotional processing, apparent throughout BD and schizophrenia episodes. Both BD and schizophrenia share thalamic and amygdalar dysconnectivity which is linked to sensory and processing stimuli. By comparing affected brain regions and disease symptoms, we can start to understand how these disorders are similar and different.

Similarities and differences between brain structures in disease

Although distinct neurological conditions, ASD and BD have shown clinical similarities in similar regions of the brain. Abnormal neural connectivity within the frontotemporal lobe and mesolimbic system can lead to emotional hypersensitivity. In turn, this hypersensitivity can inhibit the lingual gyrus' high-order processing in the brain. As a result, this inhibition can cause

incomprehensible behavior that has no accomplish goal orientation, which validates a person's sense of self-worth. Interpersonal hypersensitivity from the amygdala can also play into the safety blanket of reliance on peers to determine self-worth. Dysfunctional thalmal and amygdalar connections can also explain the sensory overwhelming shown in manic episodes and ASD stages from external stimuli (8).

ASD and BD also show differences in sensitivity and behaviors. In sensory processing in ASD, certain cues and triggers can lead to sensory overload and can obtain a response to environmental stimuli in all five senses and produce an avoidant response to overwhelming triggers (4). This can be traced back to the thalamic and amygdalar dysconnectivity producing the hypersensitivity to triggers. In BD, it's more common for individuals to regulate more specific triggers and be overall less avoidant, although this varies from episode to episode (3). ASD does not have full-on manic episodes whereas BD is more patterned and can show similar cycles in symptoms with each episode, as the disorder progresses.

ASD and schizophrenia show similarities in neural mechanisms and behaviors. Impulsive behaviors and loss of judgment from the PFC can be seen in schizophrenic episodes and psychotic symptoms in some ASD individuals (10). The amygdala may heighten sensory hypersensitivity with difficulty in processing stimuli in reality and produce heightened emotions (10). However, both are distinct and the manifestation of symptoms are different between diseases. hallmark of psychotic symptoms commonly found in schizophrenia from irritation cannot manifest in psychotic symptoms in individuals with ASD.

Both mental health disorders, BD and schizophrenia, also show various similarities. The connection between the mesolimbic region and the dopamine pathway can lead to dysfunctional circuits and an imbalance in dopamine levels (8). This can then contribute to the development of negative symptoms and depressive states along with anhedonia-like symptoms. Impulsivity may be heightened and risk-taking behaviors may be unconsidered with a dysfunctional PFC. Individuals may also portray heightened emotional responses, threat perception from social cues, or paranoia from delusion (24). Despite these similarities, there are differences in the onset of the illnesses and what symptoms may manifest throughout. In BD, manic episodes can last for at least a week whereas mania-like symptoms in schizophrenia persist for the duration of the disease and are less episodic (17). Examining brain regions can inform our understanding of how the brain malfunctions in these disorders and diseases, but in order to understand why the cells in the brain are less connected, we must turn to genetics.

Underlying genetics

ASD and schizophrenia risk factors stem from the environment. Individuals with schizophrenia show an increased risk for bipolar disorder. Both show de novo point mutations (mutations that show up within one individual) are present in genes coding for synaptic proteins, which are responsible for neurotransmitter release and primary development of branches (axons and dendrites) in neurons (20). Alongside this mutation, there are aggregative high-risk alleles from structural mutations (CNVS) and missense point mutations that may contribute to a higher

frequency of risk alleles. In a study with 3,000 Europeans, several deletions were found at *NRXN1*, an underlying genetic risk factor linked to schizophrenia and found in ASD (20). Neurexins are found in the presynaptic terminals of neurons and are pre-synaptic adhesion molecules that bind across synapses to neuroligins via alternative splicing to promote synaptogenesis with present neuroligins on nearby neurons (20). They are essential for excitatory and inhibitory synaptogenesis and maturation of synaptic connections (20). ASD patients also show chromosomal deletions/duplications at *NRXN1*. With a disrupted coding sequence, there are structural mutations that can lead to losses in function. Overall, ASD individuals have high frequencies of de novo deletions and mutations in their genome that may be linked to their symptoms. As genetic dispositions continue to be discovered, the likelihood of diseases like ASD being associated with other diseases grows.
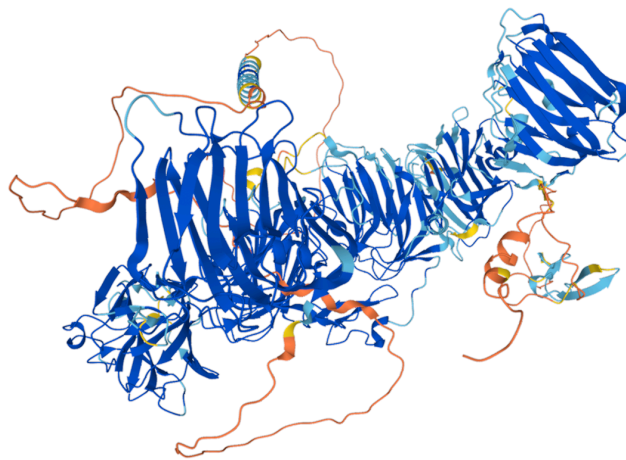
Figure 2: With deletions in NRXN1 proteins, there is a higher risk of the development of ASD. (39).

Conclusion

Although it is not fully understood why all three disorders present similar symptoms, genetic factors and brain structure could be responsible for some of these similarities. They all share common symptoms that can be altered with these environmental factors. In turn, genetic dispositions, such as mutations in the *NRXN1* gene, can indicate presynaptic and postsynaptic synapse abnormalities, resulting in less synaptic connections within the neuronal terminals. With less connective bindings, there is less proficient signaling and more intellectual debilitation. Through reduced gray matter found in resting state MRIs and gray matter MRIs, images show less matter in the brains of those with onset schizophrenia and BD. Between the two, the main areas highlighted in resting state MRIs pointed to mesolimbic and amygdalar dysconnectivity. Such disconnectivity could prove less sensory interpretation and emotional processing found in BD and schizophrenia patients. Not only this, but the sensitivity to symptoms may become heightened with hyper or hypoactive changes to the brain coming from abnormal structure. Symptoms in particular like hallucinations may become comorbid in patients with BD or autism simply due to any similar structural anomalies that have continued to progress over time (13).

Although they may manifest differently from person-to-person it all proves a relationship between how structure equates to the function within the body. This imaging furthers how no brain is made the same, but through structural and neuronal abnormalities, there is heightened sensitivity and increased likelihood of comorbidity in the three disorders.

Shared symptoms across Bipolar Disorder (BD), schizophrenia, and Autism Spectrum Disorder (ASD) suggest the significance of genetic factors and brain structure in their development. Genetic predispositions, such as mutations in the *NRXN1* gene, show synaptic abnormalities that may lead to reduced synaptic connections and cognitive impairment. Structural abnormalities, particularly in gray matter, appear to cause altered sensory processing and emotional responses. With such information, new technologies and medications can aim to reduce the severity of symptoms associated with all three disorders. With such, effective therapeutic strategies could significantly improve the quality of life for individuals affected by these conditions.

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The Emerging Role of Oligodendrocytes in Alzheimer's Disease By Arjun Gurjar

Abstract

Alzheimer's Disease (AD) is a neurodegenerative dual proteinopathy that is traditionally described by a cascade of neuronal death. More recently, glial cells such as microglia and astrocytes have emerged as key modulators of neuroinflammation and AD pathology. However, the third major CNS glial cell, oligodendrocytes (OLG), have gone under-recognized for their role in white matter AD pathogenesis. This paper outlines three different areas of OLG or oligodendrocyte precursor cell (OPC) involvement. First, oxidative stress inhibits OPC differentiation into mature OLGs and also inhibits proliferation. Second, demyelination is involved in a cyclical model leading to iron-mediated protein aggregation and further demyelination. Lastly, OPCs and OLGs are involved in complex inflammatory signaling pathways and contribute to microglial activation and neuronal excitotoxicity. In essence, OPCs and OLGs are crucially involved in AD progression and may even play active roles in protein aggregation, seeding, immune activation, and other facets of the disease.

Intro

Alzheimer's Disease (AD) is a neurodegenerative dual proteinopathy that is characterized by amyloid-beta (Aβ) aggregates and tau neurofibrillary tangles. AD has traditionally been understood from a framework of neuronal malfunction due to protein aggregates inhibiting synaptic transmission, inducing cytotoxicity, and destabilizing neuronal axons (1-2). However, more recent research has shown that non-neuronal matter, namely glial cells, are also deeply implicated in its pathology. Glial cells are a non-excitable type of cell matter that are responsible for many functions, including synaptic pruning, regulation of the neuronal environment, formation of the tripartite synapse, Ca^{2+} uptake, regulation of the blood-brain barrier, phagocytosis of apoptotic cells, metabolic support, and myelination of neurons (3-5). Oligodendrocytes represent the majority of glial cells in the central nervous system (CNS), but the focus of glial-related AD clinical therapies and research has been on other glial subtypes: astrocytes and microglia (6-8). Mounting research suggests that oligodendrocytes play a significant role in neurodegenerative pathology and may possess a causal role. In a healthy brain, mature oligodendrocytes are responsible for the myelination of the axons of neurons to enable the characteristic saltatory conduction as well as the metabolic support of axons (9-10). Oxidative stress, age-related DNA damage, and disease-specific conditions can all affect myelination by preventing oligodendrocyte precursor cells (OPCs) from differentiating into myelinating oligodendrocytes and may induce OPC death (11-17). A decreased oligodendrocyte count or demyelination can lead to neuronal degeneration and axon loss (18). This review discusses the role oligodendrocytes play in facilitating AD pathology through three main pathways: OPC dysfunction, demyelination and OLG dysfunction, and neuroinflammation.

In the formulation of this review, an extensive PubMed search was conducted to elucidate the role of oligodendrocytes in AD pathology. The initial filtering of articles was based on

analysis of methodology, year of publication, and use of orthogonal validation techniques. Papers with sufficient mechanistic insights were then reviewed in further detail..

Alzheimer's Disease Pathology

AD is a neurodegenerative disease characterized by prolonged neurodegeneration that emerges in the entorhinal cortex or hippocampus (19). There are many genetic risk factors for AD, including variations of the APOE ε4, AAP, Presenilin1, and Presenilin2 genes (19). Further, several environmental factors, as well as brain trauma, cardiovascular disease, and depression, can predispose individuals (19). Recently, cerebrospinal fluid (CSF) samples obtained via spinal tap with low Aβ42 and increased tau levels have been shown to effectively diagnose patients in the preclinical stage (19). AD is characterized by extracellular Aβ plaques and intracellular neurofibrillary tau tangles (2). Most commonly, pathology is described by the amyloid cascade hypothesis, where patients exhibit a long asymptomatic phase followed by a neurodegenerative cascade (2).

Amyloid-Beta

Many Aβ peptides are derived from the cleavage of the transmembrane protein APP via alpha, beta, and gamma-secretase. When APP is cleaved by alpha and gamma-secretase, amyloid-beta 42 (Aβ42) is produced (19). Aβ42, the most fibrillogenic (fibril forming) amyloid species, forms cytotoxic aggregates that themselves produce toxic Aβ42 oligomers that cause synaptic loss and cell death (2). These oligomers also function as nucleation sites for fibril formation in other areas of the brain (2). There are two main types of amyloid plaques, diffuse and dense core. Diffuse plaques consist of Aβ but are not involved in pathology as much as dense core plaques. Dense cores are positive for tau neurites as well and are involved in synaptic loss. Overall, dense cores are more correlated with disease intensity (2). From a clinical perspective, Aβ targeting drugs and immune therapies have shown variability in effectiveness, and many trials have been poorly designed (20). Furthermore, validation of the amyloid cascade hypothesis in animal models has been difficult to obtain, and while it has not been invalidated, it has not been substantially supported as the leading cause of AD either (20).

Tau

Tau is a microtubule-associated protein that confers microtubule stability along axons, allowing for axonal growth and other vital properties (2). When tau is hyperphosphorylated—containing 5-9 phosphates as opposed to 2-3 in normal tau —tau proteins decouple from their microtubules resulting in the formation of insoluble neurofibrillary tangles (NFTs), which can affect axonal transport in both early and late-stage AD (21-22). However, research indicates that the more substantial impact of tau is mediated by the dissociated tau oligomers prior to NFT formation (23). These toxic oligomers induce neurotoxicity and affect synaptic plasticity and long-term potentiation, as well as seed the accumulation of native tau into neurotoxic aggregates (23). In line with this property, tau has been shown to exhibit prion-like

propagation in the brain. Additional filament formation was induced in healthy, full-length tau via cellular uptake of hyperphosphorylated tau filaments (24). Additionally, Aβ and tau interact, which further promotes neural dysfunction (25). Tau and Aβ mutually suppress the expression of regulatory synaptic genes and exhibit a joint hyperactive phenotype (26).

Inflammation

Several studies in the last forty years have reported the colocalization of immune activity and Aβ plaques and have noted that the administration of anti-inflammatory drugs exhibited neuroprotective effects (27). Inflammation seems to be a protective innate immune response in the early stage that becomes pathological when inflammation becomes chronic (27). Specifically, microglia, which are the brain's subpopulation of immune cells, seem to perpetuate the chronic immune response via inflammatory cytokines, reactive oxygen species (ROS), and reactive nitrogen species (RNS) (27). Further, inflammation seems to propagate Aβ deposition and promotes tau hyperphosphorylation via interleukin-6 (Il-6) dysregulation of the CDK5/p35 pathway (27). The initial brain immune response promotes Aβ clearance via microglial phagocytosis, but after prolonged inflammation, Aβ deposition is increased, and microglia exhibit reduced clearance efficiency (27). Further, chronic activation of microglia leads to a cyclical progression wherein microglia release neurotoxic immune markers, which leads to neuronal death and further microglial activation (28).

Oligodendrocytes

Derived from "cells with few branches" in Greek, oligodendrocytes are morphologically characterized by small spherical nuclei with several processes extending from their soma, the cell body (29). Oligodendrocytes are primarily found within the CNS and primarily proliferate in the ventral ventricular zone (VVZ) in the spinal column and subventricular zone (SVZ) in the forebrain (29). Oligodendrocyte maturation lineages begin with neural stem cells that then differentiate into glial-restricted progenitor cells (29). These OPCs are also known as NG2+ glia due to the presence of NG2 proteins on their cell surface (30). While some OPCs can remain undifferentiated and become mature OPCs, the majority migrate out of germinal centers in the brain and differentiate into myelinating oligodendrocytes (30). OPC migration is mediated by secreted chemical factors such as platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), and hepatocyte growth factor (HGF), as well as extracellular matrix proteins and cell surface proteins (29). OPC differentiation is mediated by many factors, most notably g-protein-coupled-receptor 37 and Gab1 (31-32). Some complications can arise from the over-differentiation of OPCs, including oligodendroglial hyperplasia, which is mediated through epidermal growth factor signaling (30). The OPCs then must be activated to begin myelinating, which can occur through neuronal electrical activity. The firing of impulses leads to the release of ATP, which antagonizes OPC proliferation and promotes their differentiation and myelinating phenotype (29).

Myelin

Myelin is an insulating material made up of fats and proteins that enables better conduction of electrical signals along axons (33). Myelin sheaths wrap around axons and are divided into segments that end at the Nodes of Ranvier. Myelin prevents the diffusion of ions from out of the axons besides focused regions and decreases capacitance across the membrane, which improves conduction speeds. Myelin also enables saltatory signaling, where signals are propagated down the axon via concentrated sodium channels at the nodes of Ranvier. Myelination might also play a role in cognitive processing. Mice with induced demyelination were compared to wild-type mice, and the mice with demyelination performed worse in auditory information processing (34). This suggests that myelin alterations could alter cognitive performance as well.

Oligodendroglial Metabolic Support

The second role that oligodendrocytes play is in metabolic support. Oligodendrocytes provide trophic support to neurons via paracrine secretion of cerebral dopamine neurotrophic factor, brain-derived neurotrophic factor, and insulin-like growth factor (5). Some forms of oligodendrocytes, called satellite or perineuronal oligodendrocytes, don't myelinate axons but rather reside in gray matter near the neuronal soma and provide metabolic support (35). These oligodendrocytes could be recruited to become myelinating if trauma occurs. Oligodendrocyte-neuron metabolic dysfunction in the pathology of AD is less reported and requires further investigation.

OPC-Aβ Pathology

OPCs appear to be integrally involved in AD pathology. Several studies have validated that OPCs exhibit altered behavior in multiple transgenic murine models of AD, and some even imply a causative role. In a triple transgene (3xTg) AD murine model, a significant decrease in OPC proliferation at 6 months as measured by OPC sister cell count. Further OPC hypertrophy and accumulation at Aβ plaques were noticed at 24 months (14). This suggests that OPC dysfunction is implicated in early pathology and precedes amyloid aggregation. The authors did not notice a significant decline in the overall OPC population until later stages of disease progression, which they attribute to impaired differentiation. Other studies that show Aβ causes oxidative stress offer an explanation for this phenomenon. Increased intracellular ROS downregulated differentiation factors such as Sox10, Shh, and HDAC3 without affecting cell viability (17). Further, histone deacetylase is associated with OPC differentiation, and the same study reported persisting histone acetylation (15-16). In a 5xFAD murine model of AD, adult OPCs exhibited altered transcriptional profiles and accumulation around Aβ plaques suggesting involvement in pathology (15). Interestingly, the quintuple transgene (5xF) AD study noted OPC transcriptional alteration seemed to be independent of Aβ pathology. Further work will need to be done to identify the time course of OPC pathology and better delineate causal factors. In an APP/PS1 murine model, decreased OPC density was observed at 9 months, and morphological

transformation was observed at 14 months with OPC dystrophy, exhibiting shrunken and fibrous processes (36). Further studies would be required to confirm whether this morphological change is correlated with proximity to amyloid plaques or exposure to soluble oligomers. In APP/PS1 mice, Aβ was found to induce OPC senescence (37). Aβ induces senescence uniquely in NG2+ and olig2 OPCs as characterized by p21/CDKN1A and p16/INK4/CDKN2A protein upregulation and β-galactosidase activity (37). When these mice were treated for senescence with a combination of dasatinib and quercetin, the authors noted decreased Aβ burden, improved cognitive performance, and reduced inflammation (37). These results highlight the therapeutic potential for senolytic drugs targeting OPCs in AD. Further, demyelination sensitized cultured oligodendrocytes from postnatal mice by increasing sensitivity to glutamate and Aβ toxicity (38). These effects were achieved through higher intracellular levels of Ca^{2+} (38). Further evidence that implies OPC is involved in AD includes the secretion of Aβ by plexin B3+ adult OPCS upon FGF2 withdrawal, a factor whose presence normally stimulates OPC proliferation and survival (39).

Myelin Pathology

Based on mounting evidence of tau and Aβ interaction with myelin, this paper suggests a crucial pathological role of myelinating oligodendrocyte dysfunction and myelin breakdown. Myelin decrease has been found to correlate with aging, as demonstrated by CSF myelin water fraction (MWF) (40). Further, lower Aβ42 was associated with lower MWF (40). A few studies have indicated that myelin basic protein (MBP), a key component of myelin, shows neuroprotective effects by binding to Aβ and preventing fibrilization (40). A study found that MBP possesses autolytic serine protease activity and degraded Aβ42 faster than Aβ40 peptides (41). MBP also degrades fibrillar Aβ (41). These results could explain the correlation between MWF and Aβ as aging-related myelin breakdown could permit Aβ pathological progression. This hypothesis is further supported by previous studies, which indicate that myelin breakdown precedes Aβ and tau pathology, implicating a causative role of myelin degradation in AD pathology (40).

However, preclinical imaging studies found that white matter inflammation and damage occurred after exposure to misfolded Aβ (42). It could be that myelin pathology and Aβ pathology emerge simultaneously or feed into each other, confounding the establishment of a causal connection. Regardless, further studies will need to be conducted in order to determine if myelin pathology precedes Aβ or tau accumulation. Analysis of CSF samples also indicated that the ratio of phosphorylated tau to Aβ and total tau to Aβ modified the relationship between MWF and age (40). Myelin breakdown and formation of Aβ plaques in past studies suggest that toxic Aβ oligomers can lead to focal demyelination at Aβ plaques (43). Myelin and oligodendrocytes have high levels of iron, with oligodendrocytes having the highest levels of iron among any neural cell type (44). Further, iron levels have been shown to increase with aging, suggesting iron is a risk factor and marker for demyelinating diseases. With myelin breakdown due to proximity near Aβ plaques, tissue iron is elevated (44). Abnormally high

levels of tissue iron have been show to produce senile plaques (44). Other studies indicate that iron retards the ordered aggregation of Aβ and thus promotes toxicity in AD (45). Further, chelation of iron was shown to increase the life span of drosophila models of AD (45). These results are inconsistent with the earlier results that iron promotes fibrilization, and further studies are required to determine the effects of iron on Aβ. However, in both scenarios, iron is oligotoxic either via promoting the formation of Aβ plaques or oligotoxic peptides and ROS. Further, oligodendrocytes are the only neural cell population to express the iron transport protein transferrin, and they also express the TIM2 ferritin transporter (46). Therefore, oligodendrocytes are a crucial component of CNS iron homeostasis, and oligodendrocyte disruption might have significant adverse impacts on AD pathology. Given these data, this paper proposes a cyclical model wherein Aβ deposition or peptide toxicity induces demyelination and oligodendrocyte death, releasing more ferritin-bound iron and inducing Aβ deposition or toxic species formation. This pathological model is summarized in Fig. 1. Further work is needed to confirm that myelin breakdown and oligodendrocyte death release iron.
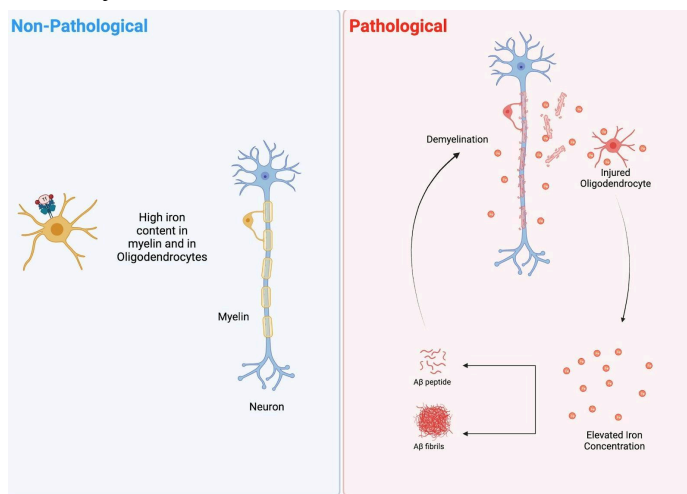
Figure 1: Cyclical model for myelin and Aβ in with myelin breakdown triggering iron release, which causes amyloid fibrillization. Created with biorender.com

MRI imaging also supports that demyelination is correlated with AD pathology (47). One study showed that clusterin, a homeostatically expressed inhibitor of differentiation in OPCs, was upregulated upon Aβ and myelin uptake (48). This supports that myelin breakdown and Aβ plaque formation lead to suppressed myelination as OPCs are prevented from maturing into myelinating OLS. This progression is facilitated by increasing axonal vulnerability due to demyelination which makes axonal degeneration more likely (18). Evidence suggests that myelin may interact significantly with tau as well. Oligodendrocytes myelinate neuronal axons by extending cellular processes that depend on microtubules. When microtubules become destabilized due to tau hyperphosphorylation, oligodendrocyte myelination can not function, which leads to ensuing neuronal dysfunction. Analysis of AD brains revealed that the activity of certain phosphatases was reduced more in white matter regions than gray matter (49). Since phosphatase counteracts the phosphorylation of tau, decreased activity might result in greater tau pathology and NFT formation. Specifically, the fact that activity was reduced further in white

matter suggests that tau pathology might be more prominent in white matter regions. In one combined MRI and PET imaging study, it was demonstrated that tau uptake was lower in cortical areas with higher levels of myelination, suggesting a neuroprotective role of myelin in preventing tau uptake (50). Another study implies a causative role for oligodendrocytes in tau pathology. Oligodendrocytes were shown to facilitate tau seeding and spreading in white matter (51). Reversal of myelin degeneration also demonstrated promise in reversing some effects of AD pathology in an APP/PS1 murine model (52). Upon introduction of a pro-myelinating drug, clemastine, the mice performed markedly better in memory tasks, indicating a potential therapeutic opportunity for myelin regeneration (52).

In light of this evidence, this paper proposes a three-pronged model for overall oligodendrocyte involvement in AD. Disrupted OPC differentiation and proliferation, demyelination and cyclical pathology, and chronic inflammatory insults recapitulate a new model to evaluate oligodendrocyte pathology in AD.

Oligodendrocytes and Neuroinflammation

Neuroinflammation uniquely affects oligodendrocytes and has been recognized as a crucial pathological element in AD. Microglial and astrocytic phenotype changes can affect neurons and OLs and might even affect myelination. The period of acute inflammation can be beneficial as it promotes wound healing and recruits OPCs to begin remyelinating via many secreted growth factors (53). Further, a subgroup of secreted factors called neurotrophins mediate neuronal and oligodendrocytic development (54). Further, TNF-α, while being pro-inflammatory, suppresses immune activity and allows for OPC proliferation and remyelination (55). Microglial inflammatory phenotype becomes deleterious when they are chronically activated. Further, OPCs exhibited diminished differentiation when the microglial secreted factor IL-1β was removed (56). Microglia that have assumed an inflammatory phenotype begin secreting pro-inflammatory factors, including ROS, reactive nitrogen species (RNS), cytokines, and glutamate (57). While the secreted factors affect all neuronal cell types, OLs exhibited greater susceptibility (57). Exposure to microglial factors leads to arrested OPC proliferation and increased cell death, as well as poorer quality of myelin produced by myelinating OLs (57). The secretion of glutamate is particularly interesting because OLs are susceptible to excitotoxicity, where glutamate signaling increases intracellular Ca^{2+} concentration leading to cell death. Further, in ischemic brain disorders, cell death leads to increased glutamate concentration leading to excitotoxicity (58). In fact, when microglia were exposed to Aβ, they released more glutamate, which could lead to OL death (58). Additionally, astrocytes, which usually clear glutamate, demonstrated impaired glutamate uptake when exposed to Aβ (59). Further work needs to be done to directly demonstrate that microglia and astrocytes can mediate OL death via excitotoxicity. Microglia also secrete many factors during remyelination that can negatively affect OPC and OL cell viability. Amongst these factors are TNF-α, TGF-β, IL-1β, and iNOS (60). Microglia were also found to communicate with astrocytes using extracellular vesicles (EVs). Astrocytes cultured with the microglial EVs assumed the A1 phenotype, which

inhibits OPC differentiation (60). Microglia also have a direct effect, however, and OLs cultured with M1 conditioned medium demonstrated reduced differentiation, and those cultured with M2 conditioned medium demonstrated increased differentiation (60). The complex interaction between microglia and oligodendrocytes emphasizes the need for a deeper understanding of their role in CNS repair and provides insights into potential therapeutic targets for AD.

Mounting evidence suggests that OPCs and OLs play more than just passive roles in neuroinflammation. This perspective is corroborated both by research in vitro and in vivo on Alzheimer's models but also from other demyelinating and neuroinflammatory disorders like multiple sclerosis (MS). Oligodendrocytes are not just bystanders to inflammatory processes but express many immune markers as well (57). OLs express MHC1 and therefore interact with CD8+ T Cells (60, 57). OLs can both be targets of CD8+ T cells and also act as antigen-presenting cells (60). In MS tissue, a subpopulation of OLs expressed the ligand for NKG2C+ CD4 T Cells, which might contribute to demyelination (61). Further studies will have to determine if OLs in AD tissue express the same ligand. OLs have a basal expression of inflammatory genes, which is significantly upregulated in a disease state. Experimental autoimmune encephalomyelitis (EAE) mice, a common model for neuroinflammation and MS, exhibit OPCS that have significantly upregulated MHC1 and MHC2 compared to controls (62). This change is mediated via IFNγ (62). OPCS also had increased phagocytic activity and were more capable of inducing CD4+ memory and effector T cell proliferation, and cytokine release. Moreover, MHC1 induces CD8+ T cell TNFα and IFNγ expression, which can lead to inhibited differentiation and increased OPC death (62). IFNγ induced OPC IL-1β expression, which leads to the astrocytic secretion of IL-6, causing suppressed OPC differentiation (62). OPC IL-1β might also increase neuronal glutamate excitotoxicity via upregulating glutamatergic signaling, leading to further neurodegeneration and demyelination (62). Further, OLs express receptors to many interleukins and chemokines and can express CCL2, CCL3, CXCL10, IL-6, and IL-8. IL-6 dysregulation is a crucial component of AD, and so OL dysfunction might contribute to AD pathology (27). Further, CCL2/3, CXCL10, and IL-8 are responsible for the recruitment of microglia so OLs might contribute to inflammatory responses (57). Further, OLs might activate microglia via secreted nucleotides that bind microglial purinergic receptors (57). Therefore, demyelination, which would release intracellular nucleotides, may activate microglia, and chronic demyelination may feed back into chronic neuroinflammation. Mice that were modified to suppress apoptotic factors in OLs exhibited greater resistance to inflammatory demyelination (63). This supports the theory that OL death can lead to further demyelination. There also is mounting evidence for the role of exosomes in glial cell crosstalk and inflammatory pathogenesis. Stressed OLs release exosomes which are uptaken by microglia resulting in phenotypic changes (57). Analysis of OL exosomes revealed that they contained ceramide and myelin protein. In a disease state, OL exosomes also contain TNF-R1 and many cytokines (57). OL exosomes have also been demonstrated to deliver neuroprotective factors to axons, and that neurons can mediate OL exosomes (64). OL exosomes are auto-inhibitory and suppress differentiation, and their release can be mediated via factors from neuronal conditioned medium

(65). Further, microglia that were cultured in conditioned medium from both proliferation and differentiated OPCs demonstrated gene expression changes in several inflammatory genes (66). Immuno-modulatory genes SOCS3 and Il1rn were upregulated with a conditioned medium from proliferating OPCs (66). Pro-inflammatory marker NOS2 was upregulated in the differentiated OPC medium, and Ptgs2 was upregulated in both media (66). The anti-inflammatory marker IGF-1 was universally downregulated (66). Moreover, microglia exposed to conditioned medium exhibited greater phagocytic tendency as measured by the percent of microbeads endocytosed (66).

Conclusion

This paper proposes a comprehensive model highlighting the significant involvement of oligodendrocytes in Alzheimer's pathology. Firstly, OPCs exhibit altered phenotypes and behavior around Aβ plaques, contribute to white matter angiogenesis, and a subset even secretes Aβ. Secondly, focal demyelination occurs around Aβ plaques, accompanied by increased oxidative damage, reduced tau uptake by OLs, and a cyclical progression involving myelin-breakdown iron release and Aβ fibrilization, further facilitating tau seeding and prion-like propagation. Considering the critical role myelin plays in neuronal health, it is imperative to recognize myelin pathology as a significant factor in AD pathology, warranting further clinical exploration. Potential clinical targets include OPC-related white matter angiogenesis, myelin-induced iron release and Aβ fibrillization, oxidative damage, and hyperphosphorylation of oligodendrocyte processes. Future studies should confirm the altered behavior of OPCs in proximity to Aβ plaques and investigate whether iron release and Aβ plaque formation indeed participate in a cyclical process. Additionally, the effects of senolytic therapies, such as clemastine, on improving cognitive performance in AD patients warrant further investigation. Lastly, OLs seem to be heavily involved in neuroinflammation, especially in models of other inflammatory demyelinating diseases such as MS. OLs seem to not only respond to inflammation but recruit inflammatory agents and release inflammatory factors themselves. Altogether, the mounting evidence underscores the pivotal role of oligodendrocytes in AD pathology, presenting new avenues for therapeutic interventions and enhancing our understanding of this complex neurodegenerative disease.

Acknowledgments

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Struggles After Success: The Relationship Between NASA and the Public/Government from 1960s - 1990s By Ashley Sang

Abstract

The success of Apollo 11 led to a widespread reaction of national pride among American citizens. Yet, critiques emerged at the beginning of the Apollo mission, arguing against the immense cost involved and the government diversion from civilian problems, which in part prompted a response from NASA in the form of the Technology Utilization Program in 1964. This program intended to respond to critics who claimed NASA was wasting public resources by using Apollo technology to solve human issues on Earth. Facing a crisis of budget deficit, President Nixon enacted several restrictive policies on NASA, causing reduced funding and a loss of prioritization. The program was later published to the public as the Spinoff reports starting in 1976, highlighting its societal impact, wide range of applications and capability of addressing civilian problems. This paper examines one of NASA's responses to President Nixon's policies and how public critique from the 1960s to 1990s affected public and government perception and how society was impacted.

Section 1: Introduction

1969 was an exciting year in space history with the success of the Apollo 11 moon landing. When the uplifting news of the moon landing spread over the U.S. on July 20, 1969, not all Americans were celebrating the success. Rather, the resentment and anger felt by many minorities caused "an estimated 50,000 people [to flock] to the Harlem Cultural Festival and [boo] in response to the moon landing"[53]. While some argue that the event temporarily distracted them from their suffering of poverty and daily struggles, some minorities, specifically black people, were frustrated, protesting that the immense money invested in the Apollo Program could have been better utilized to rehabilitate cities. The newspaper "Black Anger" by Thomas Johnson argues the deep alienation that minorities felt towards a society that prioritizes issues such as the Vietnam War[1]. They argued that the space race trivialized civilian problems such as social and economic inequality[54]. The successful moon landing demonstrated that Americans were capable of achieving ambitious goals, but it also brought attention to the nation's failure to effectively address problems such as discrimination, hunger, and malnutrition. To stay relevant and gain support from the public, NASA initiated the spinoff program to show society the practical applications of their technology. Even today, the program transforms aerospace technology into consumer products and issues an annual magazine: *NASA Spinoff Report*.

The birth of the program is highly related to the Apollo 11 mission, which had a resounding impact on society. Accomplished during the heat of the Cold War, the mission established US dominance in space and helped regain the faith of the American people. However, not only did it symbolize a pivotal moment in the history of humanity, marking a

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[53] Johnson, Thomas A. 1969. "BLACK ANGER." The Times of India (1861-2010), Aug 08. https://www.proquest.com/historical-newspapers/black-anger/docview/506696669/se-2
[54] "BLACK ANGER."

significant turning point for space exploration, but also the technology used during the mission made a notable impact. For example, the Apollo Guidance Computer (AGC) was the first to implement integrated circuitry, which used the computer chip. Integrated circuits allowed for a 40% reduction in space while increasing the computer's speed by 2.5 times[55]. The AGC processed data from dozens of sensors, and directly from Mission Control[56]. In addition, the AGC kept the spacecraft on track and was even capable of piloting the entire craft through autopilot[57]. Another significant piece of technology on the Apollo 11 rocket was the Display and Keyboard (DSKY) instrument panel, which communicates between the astronauts and the AGC. The astronauts would enter numbers into the keyboard as strings of code, which would be carried out by AGC[58]. Both the AGC and DSKY contributed to the development of modern-day computers and accelerated the path to the digital age[2]. Along with others, the technology on the Apollo mission was one of the most advanced at the time and still carries a resounding impact today.

The public's reaction to the moon landing was mixed with a majority expressing positive reactions, especially Americans who were ecstatic and shared the same joy as the astronauts involved in the Apollo 11 mission. In fact, police reports detail that during the moon landing, streets were eerily quiet due to citizens staying at home or in public places to watch the mission[59]. The same sentiment was shared internationally, and the US received congratulations from countries that had diplomatic relations with the US[60]. However, these positive reactions were short-lived, and NASA soon began to lose support due to a lack of public relevance and failed space missions. Failures such as the Challenger explosion led to a decline in public support and even temporarily suspended the space shuttle program which tarnished NASA's reputation[61].

However, this paper fails to explore the diversity of public opinion such as racial and cultural factors, and does not investigate the impact of governmental policy and social media on public perceptions. Furthermore, James Kauffman's study reveals how NASA's overselling of the Hubble telescope's capabilities and its ineffective communication with the public about its mission tarnished NASA's public image, leading to Congress holding hearings on its troubles and questioning NASA's credibility as well as calling for investigation panels to question NASA's

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[55] "The Technology It Took To Get To The Moon." Science Museum. Last modified June 14, 2019. Accessed July 14, 2023.
https://www.sciencemuseum.org.uk/objects-and-stories/technology-it-took-get-moon#:~:text=The%20computing%20technology%20behind%20the%20mission&text=The%20Apollo%20Guidance%20Computer%20.
[56] "The Technology It Took To Get To The Moon."
[57] "The Technology It Took To Get To The Moon."
[58] "The Technology It Took To Get To The Moon."
[59] Smithsonian. "Apollo 11 and the World." Air and Space Museum. Last modified July 15, 2009. Accessed July 14, 2023.
https://airandspace.si.edu/stories/editorial/apollo-11-and-world#:~:text=The%20flight%20of%20Apollo%2011,how%20strong%20the%20enthusiasm%20was.
[60] "Apollo 11 and the World."
[61] Hogeback, J.. "7 Accidents and Disasters in Spaceflight History." Encyclopedia Britannica, July 13, 2016.
https://www.britannica.com/list/7-accidents-and-disasters-in-spaceflight-history.

management[62]. This paper primarily focuses on anecdotal evidence and quotations from limited sources such as the Space Telescope Science Institute, which restricts the scope of research and raises concerns about reliability. Alan Steinberg's work claims that public opinion about space exploration has an impact on NASA's budget, but the relationship occurs sporadically rather than consistently[63]. The policy funding seems to be both responsive and non-responsive at the same time. Nevertheless, the relationship between public perception and NASA's budget is not certain.

Moreover, there is a lack of articles discussing how the public responded to the Spinoff program. Research done by Douglas Comstock and Daniel Lockney discusses the role of the Spinoff program, which began in 1976 and showcased examples of consumer products based on NASA technologies to educate the media and the public about the benefits of NASA's research[6]. It resonates with the public, demonstrating the tangible benefits of investing in space exploration. However, this paper does not explain explicitly how the public responded to the Spinoff program.

Based on the papers discussed above, public opinion does not have an impact on NASA's budget and space policy. The public critiques were primarily focused on NASA's allocation of a significant amount of budget to space exploration instead of addressing pressing civilian issues on Earth, such as poverty. Additionally, Johnson's government also cut NASA's budget after the explosion of Apollo 1[64].

In this paper, I collect my primary sources from a variety of archives such as NASA and various newspapers. The latter gave me insight into public opinion and NASA's responses during the Apollo mission and post-Apollo era. The location of the articles in the newspaper, such as in a headline or towards the end, also reveals how much society cares about the topic. For example, a headline would signify that the public cared greatly about NASA. However, an article near the back of the newspaper would signify that the public did not care that much about the topic, and NASA was losing relevance.

NASA's responses to criticism and reasons behind their policies are shown in NASA archives, especially from their history department. Sources such as conference proceedings and technical reports specifically outlined NASA's priorities, concerns, and plans. These sources provide valuable insight into NASA's thinking process during this time.

I collected my secondary sources from scientific journals such as Scientific American and Science Direct, searching for papers relating to the change of public opinion on NASA. Studying these sources inspires me about other historians' perspectives on the field, aiding me to form my own viewpoints.

Section 2: NASA From 1969-1980s
A. The Apollo 11 Mission

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[62] "NASA in Crisis: The Space Agency's Public Relations Efforts Regarding the Hubble Space Telescope." Public Relations Review 23, no. 1 (March 1, 1997): 1–10. https://doi.org/10.1016/S0363-8111(97)90002-3.
[63] "NASA in Crisis: The Space Agency's Public Relations Efforts Regarding the Hubble Space Telescope."
[64] Divine Robert, "Lyndon B. Johnson and the Politics of Space," Project Muse (University Press of Kansas, 1987), https://muse.jhu.edu/pub/266/edited_volume/chapter/2881361/pdf.

1. The Significance of the Apollo 11 Mission

The Apollo 11 mission is one of humankind's most impressive achievements. The Apollo 11 mission implemented groundbreaking technology such as AGC and was the first space mission broadcasted on television. It marked the definite defeat of the Soviet Union in the Space Race. For six years, both nations had competed for dominance in the space race. When former President John F. Kennedy pledged to land a crewed mission on the moon; the Soviet Union had recently put the first man, Yuri Gagarin, into orbit[65]. This success clearly distinguished the Soviet Union as more technologically advanced than the United States. Before that, the Soviets had beaten the United States in being the first to launch a human-made object into space. Moreover, the general US public was upset with the government regarding the Vietnam War. The slipping American morale and loss of faith in the US government required the U.S. to address the Soviet's technological superiority and boost national confidence. Therefore, Kennedy pledged to land a crewed mission on the Moon. When the US landed Apollo 11 on July 20th, 1969, not only did it mark a significant milestone in human history, but it also restored American faith in the government by winning the Space Race.

The Apollo 11 mission had a significant impact on the scientific community. One scientific objective of the mission was to collect moon rock samples to be studied back on Earth[66]. The moon rocks collected over fifty years ago are still being studied today, advancing our knowledge about lunar history, lunar geology, and the evolution of the solar system. They are also studied in various science fields such as engineering, materials science, chemistry, and biology[67]. Other rocks collected from the moon may be the first terrestrial meteorites from Earth, expelled almost four billion years ago during the creation of Earth itself[68]. These treasured collections have given scientists a multitude of knowledge about the creation of both Earth and the moon. Moreover, lunar observations were conducted on Earth before the moon landing. The Apollo 11 mission allowed scientists to confirm theories such as the origin of the moon. The Apollo 11 landing site has given scientists insight into the rate of crater formation, which enables scientists to predict the age of any lunar locations on the site[69]. The Apollo 11 mission has made a lasting impact on both society and the scientific community.

2. Public Reaction to the Apollo 11 Mission

The public reaction after the event was mixed instead of expected widespread pride. Undeniably, a portion of Americans were ecstatic, with "eerily quiet" streets during the night of the moon landing according to police reports[70]. However, Fig.1 shows that the percentage of people who believed that the Apollo mission was worth the cost decreased from 53% in 1969 to

[65]"Lyndon B. Johnson and the Politics of Space,"
[66] Chodos, Alan. "This Month in Physics History." Www.aps.org, Jan. 2001, www.aps.org/publications/apsnews/200101/history.cfm. Accessed 20 July 2023.
[67] "This Month in Physics History."
[68] "This Month in Physics History."
[69] "This Month in Physics History."
[70] "Apollo 11 and the World."

38% in 1971[71]. The continuation of the Apollo program, even in the midst of public disapproval shows that the purpose of the Apollo program was actually to win the Space Race and appease the government, who had likely been pressuring NASA to land a man on the moon.
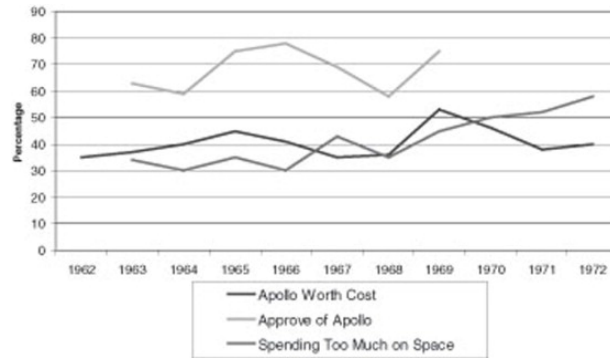
FIG 1. The percentage of public opinion of various aspects of the Apollo Program[72]

The decline of public support for NASA gave rise to various critiques from different groups and perspectives. The success of the moon landing has a multifaceted and profound impact on the poor. On the one hand, the flight of Apollo 11 can be seen as an inspiration and motivation for the poor that distracts them from their daily struggles such as poverty and hunger. On the other hand, this launch may further deprive them of their basic needs since a significant amount of resources is allocated to the program[73].

"If we can put men on the moon, why can't we build adequate housing? Or feed all citizens adequately? Or end social and economic injustices?[74]" The success of the moon landing proved that those upper-class Americans, mostly white Americans, were able to complete whatever they committed to do, but the civilian problems of the nations remained unsolved. African Americans were disappointed about the focus of the government, arguing that more attention should be put on problems happening on the Earth like racial inequality and poverty.

"A rat done bit my sister Nell.
(with Whitey on the moon)
Her face and arms began to swell.
(and Whitey's on the moon)
I can't pay no doctor bill.
(but Whitey's on the moon)
Ten years from now I'll be payin' still.

[71] Launius, Roger D. "Public Opinion Polls and Perceptions of US Human Spaceflight." Space Policy 19, no. 3 (August 1, 2003): 163–75. https://doi.org/10.1016/S0265-9646(03)00039-0.
[72]"Public Opinion Polls and Perceptions of US Human Spaceflight."
[73] Woolfolk, Evelyn. "ABERNATHY AT THE MOON LAUNCH." Sacramento Observer (1968-1975), Aug 07, 1969. 5, https://www.proquest.com/newspapers/abernathy-at-moon-launch/docview/370734716/se-2.
[74] Hoffer, Eric. "Nation: THE MOON and MIDDLE AMERICA." Time, August 1, 1969. https://content.time.com/time/subscriber/article/0,33009,901158-1,00.html.

(while Whitey's on the moon)''-Gil Scott-Heron[75]

Furthermore, the success of the moon landing highlights the problem of social inequality. The black poet Gil Scott-Heron argues racial inequality and expressed this in the form "whitey on the Moon" which tells a story about the unaffordable medical costs of being bitten by a rat, while the subject (Whitey) was sent to the moon.

B. The Challenger Disaster
1. Cause of the Challenger Disaster

After the Apollo mission, NASA attempted the Challenger Missions, a series of manned space flights initiated in 1983. The last Challenger mission launched on January 28, 1986, which exploded, carried a high school teacher Christa McAuliffe. Due to a failure of the first and second O-rings on the Solid Rocket Booster on the right-hand side, the Challenger exploded, which killed all seven crew members on board, sending the country into mourning[76]. The O-rings were designed to prevent exhaust gasses from escaping the booster but were sensitive to temperature. The tragedy happened after the O-rings became brittle after an especially cold night, in addition to erosion from previous missions[77]. The combination of factors made the O-rings particularly weak and dangerous. Therefore, when a jet of hot gas escaped through a crack in the O-rings, it punctured the fuel tank in a split second[78]. The hydrogen and oxygen from the leaked gas and fuel tank mixed, and the Challenger exploded 73 seconds into its flight[79].

2. NASA's Response to the Challenger Disaster[80]

In response to the Challenger explosion, NASA immediately inspected the Challenger rocket and began approximately 400 changes to safety, especially in the rocket boosters. A third layer of O-rings and electric heaters were added to the Solid Rocket Boosters to prevent O-rings from freezing overnight. Tiles that protected the shuttle from extreme heat during reentry were also replaced with insulation blankets. Major safety changes were made to the shuttle, such as an escape system in the case that a crew had to bail out into the ocean. Latches were also added to prevent premature interruptions to fuel flow to the engines in the fuel lines, as well as improvements to brake and steering controls.

3. Public Reaction to the Challenger Disaster

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[75] Alexis C. Madrigal, "Gil Scott-Heron's Poem, 'Whitey on the Moon,'" The Atlantic, May 28, 2011, https://www.theatlantic.com/technology/archive/2011/05/gil-scott-herons-poem-whitey-on-the-moon/239622/.
[76] Soule, Ralph. "HRO 11: Case Study-the Challenger Launch Decision." Ralph Soule, 8 Jan. 2023, www.ralphsoule.com/blog/2023/1/8/case-study-the-challenger-launch-decision. Accessed 22 July 2023.
[77] "HRO 11: Case Study-the Challenger Launch Decision."
[78] "HRO 11: Case Study-the Challenger Launch Decision."
[79] "HRO 11: Case Study-the Challenger Launch Decision."
[80] "HRO 11: Case Study-the Challenger Launch Decision."

The death of Christa McAullife in the explosion shocked her students who had been chanting Christa's name in pep rally style just before the mission[81]. They quickly found themselves in tears as they watched the shuttle burst into flames[82]. People who were in the same selection program as McAuliffe felt similarly to her students. One candidate described seeing the explosion as "getting a message your whole family was killed"[83]. Looking at public reaction in a wider range, public willingness to travel into space decreased significantly after the Challenger disaster, likely due to fear. Fig. 2 shows a set of polls conducted from 1981-1994, the public was asked whether or not they were willing to travel to space. From November of 1982 to March of 1988, public unwillingness to travel to space increased by 12%[84]. Before the Challenger explosion, the public had been under the impression that space flight was perfectly safe, due to the way that NASA advertised space flight, which was something that would be as normalized as flying in an airplane. Although the majority of the public never wanted to go to space, this data shows that the public likely lost even more faith in the safety of space flight. In another set of polls conducted from 1969-1999, opposition to funding human trips to Mars also increased after the Challenger disaster. Opposition increased from 54% in July 1969 to 59% in July 1989 and continued to increase to 64% in May, 1991 as can be seen in Fig. 3[85]. These polls show that the public was scared of going to space and likely lost faith in NASA after the Challenger explosion.
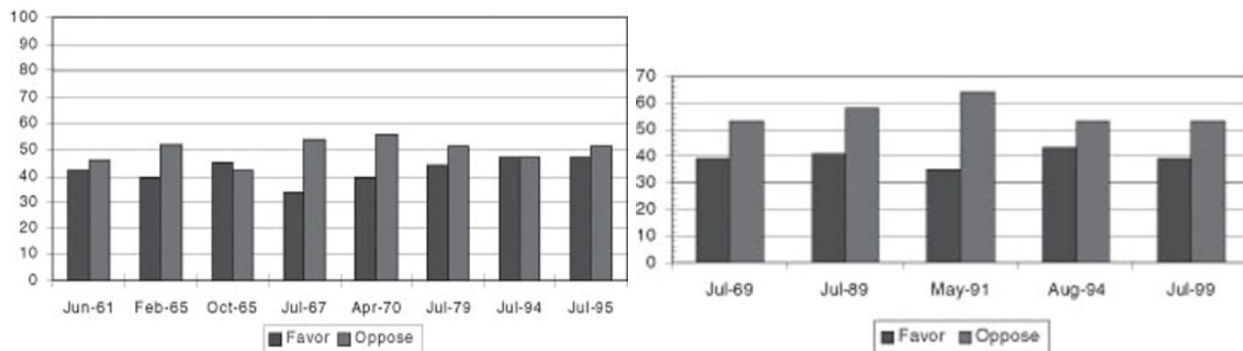
Fig 2 and Fig 3[86]. Left: The public opinion on the government's decision to fund manned flight to the moon from June 1961 to July 1995; Right: The public opinion on the government's decision to fund manned flight to Mars from July 1969 to July 1999.

4. Public Critiques of NASA and Its Impact on NASA's Budget

Although the success of the moon landing earned NASA a renowned reputation, the subsequent budget cut and pressure from the U.S. government and the public partially

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[81] "Challenger Disaster: World Reacts in Sorrow - UPI.com." UPI, www.upi.com/Top_News/US/2016/01/28/Challenger-disaster-World-reacts-in-sorrow/4011453833608/#:~:text=At%20Concord%20High%20School%20in.
[82] "Challenger Disaster: World Reacts in Sorrow - UPI.com."
[83] "Challenger Disaster: World Reacts in Sorrow - UPI.com."
[84] "Public Opinion Polls and Perceptions of US Human Spaceflight."
[85] "Public Opinion Polls and Perceptions of US Human Spaceflight."
[86] "Public Opinion Polls and Perceptions of US Human Spaceflight."

contributed to NASA's several failures, including the explosion of the Challenger, the insensitivity of the Hubble Space Telescope, and the agency's inability to design a space station. These failures tarnished NASA's public image, and reports done by researchers criticized NASA as "fossilized, overcautious, and bureaucratic"[87]. The bureaucracy of NASA increased as shown by "excessive paperwork and a preoccupation with official procedures"[88]. A substantial portion of NASA workers agreed the amount of paperwork was steadily increasing since they came to work for NASA, around 81% during Apollo and 57% post-Apollo[89]. While there was an increasing percentage of NASA scientists and engineers working for NASA, from 41.4% in 1967 to 49.9% in 1979, the promotion rate sharply decreased from 17% in 1969 to 8.3% in 1979[90]. In contrast, the promotion rate for professional administrators was significantly higher than that of scientists. From 1969 to 1979, the promotion rate was roughly around 17.0% while the percentage of workers remained relatively stable at around 15%[91]. The unequal distribution of promotion rates and the great differences in the numbers of workers further caused the bureaucracy of NASA.

Critiques from the public were unlikely to have any significant impact on the budget that NASA received. During the Apollo mission, the continuation of the mission was mostly driven by political considerations instead of public perceptions[92]. With the end of the Apollo mission, the president's control of the space program was gradually dissipating[93]. However, regardless of the change in public perception after the mission, the annual budget that NASA received remained relatively stable. Thus, public perception has a limited impact on the budget. On the other hand, the public perception may have an impact on the focus of the government. President Nixon had initiated a space program group led by Vice President Spiro Agnew[94]. A report presented on September 15, 1969 regarding the public's opinion of the Apollo mission, wrote "The attitude of the American people has gradually been changing and public frustration over Soviet accomplishments in space, an important force in support of the Nation's acceptance of the lunar landing in 1969, is not now present"[95] and "new Soviet achievements are not likely to have the effect of those in the past[96]". A majority of Americans were less interested in the success of

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[87] Arthur L. Levine, "Introduction," Public Administration Review 52, no. 2 (1992): 183–86, https://www.jstor.org/stable/976472.

[88] McCurdy, Howard E. "Organizational Decline: NASA and the Life Cycle of Bureaus." Public Administration Review 51, no. 4 (July 1991): 308. https://doi.org/10.2307/976746.

[89] Walter A Mcdougall, The Heavens and the Earth : A Political History of the Space Age (New York: Acls History E-Book Project, 2005).

[90] The Heavens and the Earth : A Political History of the Space Age

[91] The Heavens and the Earth : A Political History of the Space Age

[92] The Heavens and the Earth : A Political History of the Space Age

[93] The Heavens and the Earth : A Political History of the Space Age

[94] Steven Dick and Roger Launius, "Societal Impact of Spaceflight," 2007, https://history.nasa.gov/sp4801.pdf. p.95

[95] SPACE TASK GROUP MEMBERSHIP, "THE POST-APOLLO SPACE PROGRAM: DIRECTIONS for the FUTURE SPACE TASK GROUP REPORT T O the PRESIDE$ L the POST-APOLLO SPACE PROGRAM: DIRECTIONS for the FUTURE SPACE TASK GROUP REPORT to the PRESIDENT TABLE of CONTENTS Page," 1969, http://libarchstor2.uah.edu/digitalcollections/files/original/20/1632/Binder1_081110135224.pdf.

[96] "THE POST-APOLLO SPACE PROGRAM: DIRECTIONS for the FUTURE SPACE TASK GROUP REPORT T O the PRESIDE$ L the POST-APOLLO SPACE PROGRAM: DIRECTIONS for the FUTURE SPACE TASK GROUP REPORT to the PRESIDENT TABLE of CONTENTS Page,"

the Apollo mission after Apollo 11. The report further claims, "The first time was enough. We know what's up there now[97]". The success of the moon landings had already represented the end and the result of the space race, and the USSR had been absent from critical and profound space events at the end of the 1960s[98]. However, although the restrictive policies and public perceptions occurred at the same time as Nixon's tenure in the government, there was no direct evidence proving that the public perception had an impact on the decision-making of Nixon.

Section 3: The NASA Spinoff Program
A. What is the NASA Spinoff Program?

The NASA Spinoff program aims to convert space technology into technology with real-life applications such as medical equipment and memory foam mattresses, also called 'spinoffs'. The intended audience is beyond just the general public, but also politicians, researchers, engineers, and many others. Beyond serving the public, the NASA Spinoff Program has also appeased the government by creating jobs and bringing in a net profit.

1. History of the Spinoff Program

Dating back to the 1960s, the politics of the space program was entangled and fluid. Overseeing the creation of NASA, the U.S. president, Lyndon Baines Johnson, pursued the unfinished goal of a manned moon landing from John Fitzgerald Kennedy. However, his attention shifted to the Vietnam War, and his deep concern about national poverty that the space efforts were diverting national resources on civilian problems and international affairs[99]. Such a dilemma in the distribution of the federal budget and the nation's attention had negatively affected the development of NASA. In 1967, a reduction in NASA's budget occurred after the combustion of the Apollo 1 when all three astronauts were killed. This decision was driven by the need to relieve the crisis of budget deficit[100].

Following Johnson's tenure, Richard Nixon enacted restrictive policies that further exacerbated the situation. Three changes were made: One, NASA was no longer a prioritized, personal organization, but rather a normal, governmental agency; two, no more challenging long-term space mission would be established as a crash program like the Apollo mission; three, manned spaceflight was no longer linked with any long-term plan[101]. The most dramatic consequence of these policies was that NASA had to compete for its budget, and space exploration lost its prioritization. As a result, the annual budget that NASA received was limited to 1% of the federal budget.

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[97] "THE POST-APOLLO SPACE PROGRAM: DIRECTIONS for the FUTURE SPACE TASK GROUP REPORT TO the PRESIDE$ L the POST-APOLLO SPACE PROGRAM: DIRECTIONS for the FUTURE SPACE TASK GROUP REPORT to the PRESIDENT TABLE of CONTENTS Page,"

[98] "THE POST-APOLLO SPACE PROGRAM: DIRECTIONS for the FUTURE SPACE TASK GROUP REPORT TO the PRESIDE$ L the POST-APOLLO SPACE PROGRAM: DIRECTIONS for the FUTURE SPACE TASK GROUP REPORT to the PRESIDENT TABLE of CONTENTS Page,"

[99] Neil M Maher, Apollo in the Age of Aquarius. (Harvard University Press, 2019).

[100] "Lyndon B. Johnson and the Politics of Space,"

[101] John M Logsdon, After Apollo? : Richard Nixon and the American Space Program (New York, Ny: Palgrave Macmillan, 2015). p.103

NASA wanted to maintain its prioritized position, "maintaining as much as possible of the large personnel and facility base developed for Apollo"[102]. As a response to Johnson's government restriction on funding, NASA transformed its aerospace technology into civilian products with the final program named Technology Utilization Program in 1964[103]. The birth of the program was to help build up the civilian world that Johnson pursued, so its specialized publications regarding these innovations were available to industries, academia, and scientists, resulting in a broad interest in adapting these innovations for commercial purposes. Later in the 1970s, the program became widely accessible to the American public by publishing an annual report named *Spinoff*[7].

2. Purpose of the Spinoff Program

The mission of the Spinoff program to, "[benefit] life on Earth in the form of commercial products"[104], is a true but narrow perspective. Based on quantitative data about the annual budget that NASA received at that time, the Spinoff Program was initiated when NASA was experiencing a cut in the organization's actual budget. From the time of the moon landing to the initiation of the program in 1976, the actual budget that NASA received had decreased from 4722 million dollars to 3269 million dollars, which is roughly a 31% decrease in the annual budget[105]. This also reflects in the percentage of the federal budget, which decreases from 3.45% to 0.98%[106]. On the other hand, based on the historical context, TUP as a whole was a response that NASA took to the restrictive policies in the late 1960s. The hidden purpose of the program was to maintain the position and budget received by NASA by showcasing the value of investment in aerospace technology to the government, aligning with the goal of the U.S. government. This is also supported by the data from after the initialization of *the Spinoff* program, which stated that the percentage of the federal budget that NASA received remained relatively stable at 1%[107].

3. Annual Spinoff Reports

In 1976, the Technology Utilization Program (TUP) changed to become the NASA Spinoff Program due to unexpected public attention to , at the time, the Technology Utilization Reports[108]. Therefore, NASA adapted the Technology Utilization Reports to be directed toward the public. The new reports are now called the *NASA Spinoff Report*. Every year, dozens of NASA's most noteworthy spinoffs are published in an annual report. Each spinoff featured has its own page which explains the original technology, as well as the spinoff's applications on Earth.

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[102] "Lyndon B. Johnson and the Politics of Space,"
[103] "Lyndon B. Johnson and the Politics of Space,"
[104] "About Spinoff | NASA Spinoff." Spinoff.nasa.gov, spinoff.nasa.gov/spinoff. Accessed 21 July 2023.
[105] Rogers, Simon. "Nasa Budgets: US Spending on Space Travel since 1958 UPDATED." The Guardian, The Guardian, Feb. 2010, www.theguardian.com/news/datablog/2010/feb/01/nasa-budgets-us-spending-space-travel. Accessed 19 July 2023.
[106] "Nasa Budgets: US Spending on Space Travel since 1958 UPDATED."
[107] "Nasa Budgets: US Spending on Space Travel since 1958 UPDATED."
[108] "About Spinoff | NASA Spinoff."

Moreover, the reports benefit society by showing the reader how the spinoffs can impact their own lives.

The annual reports themselves have also changed over time . In more recent reports, the purpose of each spinoff is detailed in-depth, as well as the most common applications the spinoff has. For example, specific companies are named and the report explains how each company uses the spinoff. Moreover, the target audience in these recent reports is the general public. However, older reports first recount significant technological development in the space industry that year before diving into how that technology will improve quality of life. There are no specific spinoffs. Instead, older reports outline how NASA technology will help solve real-world problems, such as shortages in a specific type of crop. The implementation of the specific technologies is also described in long articles instead of short paragraphs.

B. NASA Spinoffs

1. Global Positioning System (GPS)[109]

Some of NASA's spinoffs are today's necessities. For example, the GPS was a NASA spinoff. The GPS, or Global Positioning System, was invented during the Sputnik era of the Cold War. Scientists discovered that they were able to track the movement of a satellite using shifts in radio signal known as the "Doppler Effect". In the mid-1960s, the US Navy was able to conduct navigation experiments by placing six satellites near the poles. They were then able to detect a submarine carrying nuclear missiles by observing the shifts in the radio signal from the submarine in only a few minutes through the Doppler effect. During the early 1970s, the Department of Defense (DoD) decided to establish a navigation system. Inspired by the US Navy, it decided to use satellites for the navigation system and sent out the first Navigation System with Timing and Ranging (NAVSTAR) satellite in 1978. By 1993, 24 NAVSTAR satellites had been sent out and the navigation system was fully operational. The GPS, which was once a spinoff, is now one of the most essential pieces of technology in today's society.

2. Memory Foam[110]

Besides the GPS, another NASA spinoff is memory foam. Originally created for NASA's airplane seats, memory foam was intended to decrease the likelihood of death in the case of an airplane crash due to its ability to absorb shock. Since the invention of memory foam, it has had applications in a wide range of fields, such as memory foam in the medical field. The medical industries purchase a significant amount of memory foam for cushions in wheelchairs and mattress pads. It is also widely used by motorcyclists and drivers to add comfort and shock absorption. NASA utilizes a memory foam base at the bottom of an obstacle course to test an

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[109] Mai, Thuy. "Global Positioning System History." NASA, 27 Oct. 2012, www.nasa.gov/directorates/heo/scan/communications/policy/GPS_History.html.
[110] Memory Foam." The History of the Influence of Space Technology, spacetechdevelopment.weebly.com/memory-foam.html#:~:text=Memory%20foam%20was%20invented%20in. Accessed 21 July 2023.

astronaut's ability to regain equilibrium after being in space. Memory foam is now a commonplace item in a household, found in pillows, mattresses, and seat cushions.

C. Impact of NASA Spinoff Program on Society

1. Public Impact of the NASA Spinoff Program

One purpose of the Spinoff program is to benefit the world by converting space technology into practical real-world applications. This has held true with over 2,000 spinoffs created since the inception of the program in 1964[111]. In a study conducted in 2011, 187 spinoffs were chosen from the 2007-2010 annual reports[112]. Out of those 187 spinoffs, 76% showed productivity and efficiency improvements, 32% showed the capability to improve quality of life, 30% could benefit the environment in some way, and 16% demonstrated the ability to save lives[113]. Through their reports, NASA has also educated the public about space technology and its application to everyday life. Some spinoffs such as the Inference Kernel for Open Static (IKOS) debugging code featured in the 2021 annual report originally used by NASA are available to the general public and have been downloaded over 1200 times since 2013[114]. The availability of these spinoffs benefits the public because they enable citizens to implement space technology into their everyday lives. Additional spinoffs such as the Ultraviolet Blocking Lenses featured in the 2010 annual report, were originally intended to protect astronaut's eyes from harmful light properties in space, but now benefit the general public's physical health[115]. Moreover, the program has had wide applications in areas such as the environment and city construction, which significantly improves quality of life. In consideration of the urban environment, NASA utilized its aerospace technology to "improve water quality and alleviate air pollution[116]" NASA engineers utilized the space capsule system to recycle atmospheric gasses to produce water by dehumidification, used Apollo fuel cells to produce additional water supply, and exploited high-sensitivity detectors to locate potential water sources[117]. The same contribution was made to solve the problem of air pollution[118]. NASA's development in the field of artificial atmosphere can be utilized to generate a clean atmospheric environment within buildings, and its gas sensing technology and monitoring devices can be utilized to detect potential contamination of industries' processes[119]. Besides the TUP, NASA cooperated with the United States Department of Housing and Urban Development (HUD) to solve the problem of

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[111] "About Spinoff | NASA Spinoff."

[112] Comstock, Douglas, and Daniel Lockney. *AIAA 2011 Quantifying Spinoff Benefits. 2011.*

[113] *AIAA 2011 Quantifying Spinoff Benefits. 2011.*

[114] ---. SPINOFF. 2021.

[115] Lockney, Daniel, et al. National Aeronautics and Space Administration Spinoff 2010 NASA TechNologieS BeNefiT SocieTy. 2010.

[116] *Apollo in the Age of Aquarius.*

[117] M.L. Feldman, L.A. Gonzalez, and A.B. Nadel, "APPLICATION of AEROSPACE TECHNOLOGIES to URBAN COMMUNITY PROBLEMS," NASA Technical Reports Server, September 23, 1965, https://ntrs.nasa.gov/api/citations/19660022604/downloads/19660022604.pdf. p.21

[118] "APPLICATION of AEROSPACE TECHNOLOGIES to URBAN COMMUNITY PROBLEMS,"

[119] Ibid, p.27-28

urban housing since 1966[120]. The NASA Spinoff program utilized aerospace technology to lower the cost of "electric power, clean water, healthy air, and waste disposal for HUD's housing prototypes"[121]. NASA's engineers established the Modular Integrated Utility System (MIUS) that efficiently used resources to decrease utility costs[122]. One product of MIUS is its generation of heat energy. MIU utilized heat generated by electricity production as well as producing hot water and power. MIU could decrease energy consumption by 38% and water consumption by 27% for residential areas with 110,000 people, an exceptional result[123].

2. Economic Impact of the NASA Spinoff Program[124]

The NASA Spinoff Program also benefited the US economy. In the same study conducted in 2011 in *AIAA 2011 Quantifying Spinoff Benefits* by Douglas Comstock and David Lockney, the spinoffs collected were also analyzed for their economic contribution. All spinoffs analyzed were expected to have quantifiable benefits in jobs and revenue. As shown in Table 1, from the 187 spinoffs, an estimated 1665 jobs were created, a 532 million dollar increase in revenue, and 4.13 billion dollars in productivity and efficiency improvements. However, it is important to note that only a small portion of spinoffs studied reported quantifiable values in the annual report. Therefore, the actual amount of revenue may be much higher. Given NASA's yearly budget of 32.41 billion dollars and the large amount of money that NASA brings in with just 187 spinoffs, it can be reasonably assumed that NASA comfortably offsets its yearly spending through the Spinoff program. This is further supported through Table 2 as shown below. As seen in 1989, NASA brought in 21.3 billion dollars in contribution to sales, 315.7 million in cost savings, and created 325,000 jobs, through the spinoff program alone. This significantly offsets their spending that year of 11.036 billion dollars. This data proves that NASA is actually benefiting the economy by creating new jobs and bringing in revenue. Therefore, the purpose of the program to create economic benefit is achieved. The spinoff program succeeded in appeasing the government by proving their economic benefit, which led to NASA's budget remaining relatively stable at 1% of the federal budget.

Table 3. This table depicts the categories where we found measurable benefits and were then able to harvest existing information.

	Jobs Created	Increased Revenue	Productivity and Efficiency Improvements	Lives Saved/Not Lost	Lives Improved
	1,665	$532M	$4.13B	695	30M
Percentage of Companies	4%	5%	2%	1%	2%

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[120] "APPLICATION of AEROSPACE TECHNOLOGIES to URBAN COMMUNITY PROBLEMS,"
[121] *Apollo in the Age of Aquarius.*
[122]Pringle, Marion. "TECHNOLOGY EVALUATION of CONTROL/MONITORING SYSTEMS for MIUS APPLICATION." NASA Technical Reports Server, 1974.
https://ntrs.nasa.gov/api/citations/19740024602/downloads/19740024602.pdf.
[123] T. E. Redding, Application of the Integrated Utilities Concept to Community-Size Developments, NASA ADS (Intersociety Energy Conversion Engineering Conference, 9th, San Francisco, 1974),
https://ui.adsabs.harvard.edu/abs/1974iece.conf..493R/abstract.
[124] *AIAA 2011 Quantifying Spinoff Benefits. 2011.*

TABLE 1. This table shows the total benefits out of the spinoffs that reported quantifiable benefits. In this table, 'Companies' refers to the spinoffs, and 'Percentage of Companies' refers to the percentage of spinoffs out of the 187 analyzed that reported quantifiable benefits.[125]

Date	Study	Methodology	Quantitative Findings	Limitations
1971	Economic Impact of Stimulated Technological Activity," Final Report, Midwest Research Institute, Contract NASW-2030	• Macroeconomic projections	• Average 7:1 rate of economic return on each dollar invested in NASA • Discounted rate of return on NASA investments of approximately 33%	• Limited to ratios of R&D expenses to national economic gains
1976	"Quantifying the Benefits of the National Economy from Secondary Applications of NASA Technology," Mathematica	• Case studies of four major NASA technology categories (cryogenics, gas turbines, integrated circuits, and NASTRAN computer system)	• $1B estimated benefit of NASA contribution to cryogenics • $5B estimated benefit of NASA contribution to integrated circuits • $111M estimated benefits of NASA contribution to gas turbines • $701M estimated benefit of NASTRAN	• Small data set, lacking comprehensive overview of full NASA technology transfer portfolio • Not sustainable • Dated • Restricted only to revenue generation • Forward-looking projections of future benefit
1976	Michael K. Evans, "The Economic Impact of NASA R&D Spending," Chase Econometric Associates, Inc., Bala Cynwyd, Pennsylvania, Contract NASW-2741	• Simulations and modeling	• Average 7:1 rate of economic return on each dollar invested in NASA • Historical rate of return from NASA R&D spending of 43%	• Focused solely on economic forecasting and projections using theoretical increases and decreases in NASA funding
1988	"Economic Impact and Technological Progress of NASA Research and Development Expenditures," Executive Summary, Midwest Research Institute, Kansas City, Missouri, for the National Academy of Public Administration	• Macroeconomic projections	• Average 9:1 rate of economic return on each dollar invested in NASA • Discounted rate of return on NASA investments ranging between 19 and 35%	• Limited to ratios of R&D expenses to national economic gains
1989	"An Exploration of Benefits from NASA 'Spinoff'," Richard L. Chapman, Loretta C. Lohman, and Marilyn J. Chapman	• Examination of 259 published Spinoff stories • Telephone interviews and inquiries	• $21.3B NASA contributions to sales • $315.7M NASA contributions to cost savings • 325,000 jobs created/saved • $365M in tax receipts	• Data set restricted to NASA Spinoff companies • Restricted to revenue from sales and cost savings
1993	"The Nature and Extent of Benefits Reported in NASA 'Spinoff'," Richard L. Chapman, Marilyn J. Chapman, Mary F. Chapman, and Jody Briles	• Examination of 353 published Spinoff stories • Telephone interviews and inquiries • Continuation of 1989 Chapman Report	• $32B NASA contribution to sales • $1B NASA contributions to cost savings	• Data set restricted to NASA Spinoff companies • Not repeated • Restricted to revenue generated and savings
1994	"The Economic Impact of the Space Program: A Macro and Industrial Perspective," prepared for Rockwell International by The WEFA Group, Bala Cynwyd, Pennsylvania	• Economic modeling	• Estimated 380,000 NASA-generated jobs by 1997 • $153.5B in GDP generated by NASA-related activity by 2000	• Restricted to job growth • Restricted to human spaceflight and ISS
1997	"Space as an Investment in Economic Growth," Henry R. Herzfeld	• Surveys • Telephone interviews and inquiries • Literature review • Case studies	• Over $1.5B in value added to 15 NASA life sciences partner firms	• Small dataset, restricted to 15 program-specific technologies • Difficulty collecting data, survey responses • Not repeated

TABLE 2. This table shows several studies that have already attempted to quantify the benefits of NASA's technology transfer program. The methodologies of each study are summarized as well as their findings[126].

3. Public Response to the NASA Spinoff Program[127]

The NASA Spinoff Program led to an increase in tolerance from the public on the expenditure of NASA, especially during the beginning years of the program. As shown in Fig 5, in polls conducted from 1959 to 1987, people were given four government programs that they believed the government should cut funding: foreign aid, military, space, and welfare. At the start of 1975, space was one of the top programs that the public believed the government should cut funding, right behind foreign aid, at 57%. However, in 1987, that percentage dropped to 12%. Despite the increase in public approval, NASA lost relevance in American society. This can most

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[125] *AIAA 2011 Quantifying Spinoff Benefits. 2011.*
[126] *AIAA 2011 Quantifying Spinoff Benefits. 2011.*
[127]"Public Opinion Polls and Perceptions of US Human Spaceflight."

likely be alluded to by the fact that the Space Race ended in 1975. The Space Race was a major source of fear in the US during the 1960s. The belief that space domination would translate into national strength intensified the race. Winning the competition would show the advantage of ideology. The US believed that by winning the space race, they would in turn free the world from the potential threat of communist takeover. Moreover, whoever won the Space Race had a huge military advantage due to satellite technology capable of spying on enemy countries. The winner also had an advantage in the case of a nuclear war because nuclear bombs were relatively small and would be hard to stop if launched from space. Therefore, already under the threat of nuclear war, the US greatly desired to win the Space Race. This desire translated over to the public, who mainly supported the Apollo program. NASA itself was created in 1958 in order to address potential Soviet dominance in space technology following the launch of Sputnik. Once the Space Race ended, there was technically no more need for NASA. This loss in relevance can be seen in Fig. 6 which asks the public how important they believed the space program was in relation to other programs. From 1988 to 1994 the percentage of people who believed the space program was important dropped from 60% in 1988 to 38% in 1994.
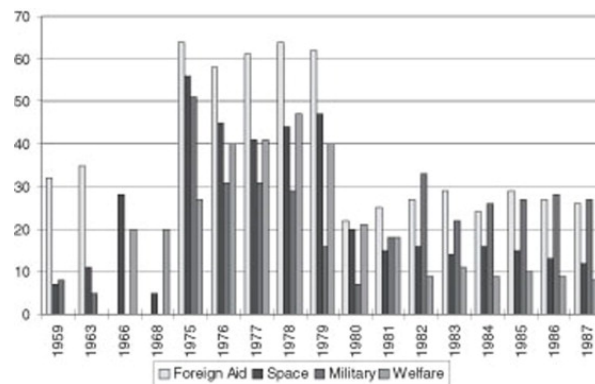
FIG 5. This set of polls shows the percentage of people who believe government funding should be decreased in various government programs from 1959 to 1987.
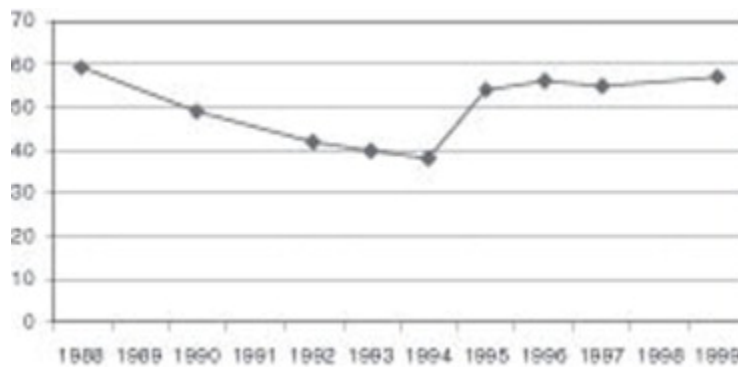
FIG 6. This table shows the change in importance the public felt NASA had to the US from 1988 to 1999.[128]

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[128]"Public Opinion Polls and Perceptions of US Human Spaceflight."

4. The Effectiveness of the NASA Spinoff Program

The effectiveness of the NASA Spinoff Program in fulfilling its mission to improve quality of life on Earth, the program was a success. Programs such as the MIU and NASA's partnership with the HUD had the potential to significantly improve quality of life. Moreover, the spinoff report educates the public about space technology and provides opportunities to apply the technology in our own lives.

However, considering that one of the NASA Spinoff Program's main goals of maintaining its prioritized position, the program's effectiveness is questioned. After the initiation of the program, NASA's funding as a percentage of the government budget increased in 1964 and 1965. However, the program was not a major factor. The percentage of the federal budget NASA received dropped significantly after President Nixon's policies despite the program. The budget was relatively stable after the initiation of the NASA Spinoff Program at around 1% of the federal budget, but the actual money received annually was increasing[129]. Some argue that money could have been directly spent on innovations and consumer goods instead of being transformed by the NASA Spinoff Program[130]. Others refute this, arguing the uniqueness of the applications requires people to think differently than they otherwise would do, regardless of the money spent[131].

Section 4: Conclusion

From the Apollo 11 Mission to the 1990s, NASA has executed several missions and programs that have all had significant impacts on society, both on the civilian front and on the economic front. Not all missions and programs established from 1960-1990 were analyzed in this report, however, the ones analyzed - the Apollo 11 mission, the Challenger disaster, and the NASA Spinoff Program - provide a good understanding of public and government perception of NASA throughout the 1960s to 1990s.

The Apollo 11 mission was a clear success for the United States, especially in terms of the Cold War. The Apollo 11 mission marked a clear success for the US in the Space Race, which secured the US as the most powerful country in the world. As NASA is a government program dependent on public support, one would assume that the public would be ecstatic at the success of the moon landing. While a portion of the public was, a larger portion believed the cost of sending humans to the moon was not worth the high taxes. This feeling was especially prominent among lower-income communities. The public also did not support the notion of the government continuing to fund human trips to the moon. This lack of support shows that the Apollo 11 mission was not for the sake of the public, but actually to appease the government in order to win the Space Race.

The Challenger disaster left a long-term effect on public willingness to travel into space. The Challenger disaster shattered the public perception that space travel was safe and was ready

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[129] Application of the Integrated Utilities Concept to Community-Size Developments
[130] McCurdy, Howard E. "Organizational Decline: NASA and the Life Cycle of Bureaus." Public Administration Review 51, no. 4 (July 1991): 308. https://doi.org/10.2307/976746.
[131] "Organizational Decline: NASA and the Life Cycle of Bureaus."

to be normalized as NASA had advertised. After the explosion, the percentage of people who were willing to go to space dropped notably. This also applied to public approval for the government to continue to fund government trips to the moon. The Challenger explosion left a fear of space travel in the public's heart.

Lastly, the NASA Spinoff program left major impacts on society and the US economy. The NASA Spinoff impacted society as many of the spinoffs were designed to improve quality of life. The NASA Spinoff program had benefited the economy, with studies showing that the NASA Spinoff program consistently offset their budget and generated a net profit. The program has also created a plethora of jobs and opportunities. Public tolerance for NASA's spending also increased, which means that public approval also increased.

By observing how the public has responded to NASA's past actions, we can predict how the public will react to NASA's future decisions. This will in turn aid us in understanding the potential impact each space mission, program or decision will likely have at an individual, societal level as well as its long term impact on technology and the economy as a whole.

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Impact of Personalized Emoji Inclusion in Mobile Banking Applications on Customer Saving Rates By Nguyen Minh Quan

Abstract

This research explores the dynamic of mobile banking applications and user's behaviors regarding financial savings. With the advancements in technology, smartphones have made things easier in that people can manage their banking and get services through their smartphones. This research specifically looks into the impact of personalized emoji messages on a mobile user's savings rate. In this case, the main objective is to determine whether integrating emojis into mobile banking application messages can positively influence users' savings habits. The research looks into a specific time of the impact, which is during the moments when a user is making significant spending and savings decisions. With the help of behavioral economics, consumer behavioral policies, and decision-making concepts, I aim to determine whether visual cues impact the financial decision-making of mobile banking application users and whether they generally positively affect their economic well-being.

Examining this research topic of interest involves adopting an experimental approach. The practical approach incorporates a control group representing a mobile banking experience without using personalized emojis. The research also includes a target group who receive targeted and customized emoji messages during important moments when making financial decisions on spending and saving. The research methodology employs both qualitative and quantitative methods of data collection. Qualitative methods include surveys and interviews to provide insights into the perception regarding their experience with personalized emoji messages. The combination of qualitative and quantitative measures provides a deep understanding of integrating personalized emoji into user behavior. This research aims to contribute to the academic disclosure of behavioral economics. Also, it provides insights for mobile banking app developers and financial institutions seeking innovative ways to influence user behavior positively.

Introduction

The financial sector is undergoing significant transformations, especially with technological advancements. Therefore, companies in this sector are forced to adapt to the changes by adopting the right strategies to keep on trend. One of the transformations is mobile banking, which enables users to access services and manage their finances from the comfort of their homes. One big part of personal finances is saving habits, essential in determining an individual's financial health. Mobile banking apps are flexible. Therefore, it allows users to facilitate transactions.

Additionally, flexibility in mobile banking can influence and guide users on critical financial choices, including saving. Therefore, financial institutions must take advantage of this flexibility and implement strategies to help their customers make sound financial decisions, especially by influencing their behaviors and managing their finances. This study focuses on one

potential strategy: integrating emojis in mobile banking applications to influence users' saving habits.

Recently, researchers have focused on studying behavioral economics more. This concept emphasizes the effectiveness of using subtle interventions to steer people to more favorable decision-making outcomes. These subtle interventions are called nudges. Nudges influence the psychological insights of an individual regarding a particular concept, which then affects their behavior in response without mandating a decision or imposing restrictions. In the case of mobile banking and managing personal finances, integrating technology-related nudges in mobile banking applications seems to be an effective strategy to influence healthy financial decisions for users. This research study focuses on a specific technology-related nudge: the incorporation of emojis in mobile banking applications. Emoji messages are visual elements used in modern communication through messaging, which have the potential to create an emotional connection. Thus, this paper aims to investigate whether incorporating personalized emoji messages to users of mobile banking applications during important moments when making financial decisions can create an emotional connection between users and their financial decisions and encourage them to improve their saving habits.

Technology evolves as time passes and impacts many organizations, including the financial sector. In the financial sector, technological advancement impacts various financial-related aspects, including how people conduct their financial transactions. In this case, it is essential to understand how technological advancements influence people's behavior in the financial sector. Integrating emoji messages in mobile banking is one of the aspects of the technical impact on the financial industry that is yet to be explored. This study, therefore, provides financial institutions with a unique strategy for fostering positive financial habits among their users. It also opens an avenue for more research study on the topic.

Literature Review

As mentioned earlier, there is limited research on the influence of emojis on people's financial decisions. This section provides a literature review of existing research studies on different aspects of this study, which include research studies on behavioral economics and nudges, emoji as nudges in financial decision-making, and studies investigating the impact of technology on economic behavior.

Behavioral Economics and Nudges

Behavioral economics is a field that uses economics and psychology to explain how people navigate and make decisions under the influence of nudges. This field acknowledges that humans make decisions based on emotions, cognitive biases, and contextual factors. In this case, nudges refer to non-regulatory approaches used to influence decisions and behaviors. Oliver (2013) illustrates how nudges work by conducting a research study on using behavioral economics in the public sector to inform the public about policies. In his research, Oliver (2013) argues that the government can use nudges to focus on changing the behavior of people who are

the subject of harm to others. In light of this, governments can choose when and how to impose direct regulations against unwanted private sector activity using behavioral economics results, such as present bias and loss aversion. This behavioral economic-informed approach to regulation is called "budge" to suggest that behavioral economics may be better applied in the public sector to help influence policies that restrict negative private sector behaviors instead of nudging citizens.

Further, another research study by Gordon & Schindler-Ruwisch (2020) on the use of nudging in the health sector shows that in a college dining hall, providing students with simple directions as interventions proved helpful in promoting healthy eating habits. In this case, nudging refers to subtle and indirect interventions designed to guide individuals toward making positive decisions without limiting their freedom of choice. The researchers implemented this approach in a college dining hall, where students often make daily food choices. The specific intervention involved providing students with straightforward instructions or cues to encourage them to make healthier choices, particularly in selecting beverages and desserts. The study's key finding suggests that these simple nudges were effective in positively influencing students' behavior. By promoting awareness and directing attention toward healthier beverage and dessert choices, the researchers observed a tangible impact on the health outcomes of the students. This implies that, in a college dining hall context, implementing nudging techniques can be a practical and successful strategy for steering individuals toward making more health-conscious decisions.

Emoji as Nudges in Financial Decision-Making

Emojis are a form of visual communication used in digital conversations using smartphones. Emojis allow people to convey their emotions in a message, which may be difficult to express through text alone. According to Bai et al. (2019), emojis are being utilized in network communication more frequently, and their applications are growing more diverse. They are closely associated with marketing, law, healthcare, and many other fields and possess distinct cognitive and emotional characteristics. Once seen as a platform for liberating voices, the digital public sphere has transformed into a complex landscape dominated by data-driven technologies. A research study by Mozdeika (2022) investigates interpassivity as a theoretical framework, challenging assumptions about users' passivity in interactive digital spaces. The paper examines how users interact with content in the digital public sphere by contextualizing the delegation of emotional subject positions within seemingly interactive activities. The review establishes a connection between the practical applications of nudges, emojis, and memes in digital contexts and the theoretical foundations of interpassivity (Mozdeika, 2022). It looks at how interactive aspects have changed, from synthetic laughter from the broadcast era to modern online responses like emojis.

Kass-Hanna and Lyons's (2022) study on behavioral economics and financial decision-making provides fundamental knowledge of the psychological influences on people's decisions. Reviewing the phenomena of irony, passionate joking, and strategic ambiguity within far-right online subcultures clarifies how these components take advantage of the interactive

nudge logic built into social media advantages. The study emphasizes how emojis are powerful communication tools that influence financial decision-making and convey various emotions (Kass-Hanna & Lyons, 2022). Expanding upon Kass-Hanna and Lyons's (2022) findings, the paper investigates how the opportunities afforded by digital media to convey genuine emotions generate an argument that users may choose to deny. This denial plays a part in unexpected events like "meme magic," which acquires symbolic significance.

In contrast to cultural participation theory, the theoretical takeaway raises the possibility that participatory culture's democratic spirit may be ironically undermined by constant engagement. Mozdeika's exploration of interpassivity and Kass-Hanna and Lyons's insights into behavioral economics and financial decision-making propose a comprehensive understanding of how emojis function as nudges in the digital public sphere. The review contributes to the evolving discourse on the intricate dynamics of the digital age by unraveling the interplay between interactivity, emotional expression, and economic choices.

Technology and Financial Behavior

The role of technology in influencing financial behavior has expanded rapidly with the digitization of financial services. Mobile banking applications, in particular, have become integral to the daily lives of individuals, offering seamless access to financial information and transactional capabilities. As users increasingly rely on technology for managing their finances, there is a growing opportunity to leverage these platforms for interventions that positively impact financial behavior. A study by Farida et al. (2021) investigates the relationship between financial literacy, the use of financial technology, financial behavior, and financial satisfaction. The findings suggest that financial literacy alone does not impact economic behavior, but financial technology does.

Additionally, financial literacy and the use of financial technology contribute to financial satisfaction, with economic behavior mediating this relationship. This study provides valuable insights into the multifaceted dynamics of individuals' financial decision-making processes in the digital age. In the context of the main topic on the impact of personalized emojis in mobile banking applications, the focus is on integrating technology (emojis) within financial services. Emojis, as a form of communication and expression, become part of the user experience in mobile banking. This personalized element introduces a novel dimension to the technology-driven financial landscape. Both studies highlight the transformative influence of technology, albeit in different forms, on economic behavior. While Farida et al. (2021) emphasize the general use of financial technology, the main topic narrows its focus to a specific aspect—personalized emojis within mobile banking applications. Both highlight the importance of understanding how technology interfaces with individuals' financial decision-making processes.

Another study by Humaidi et al. (2020) explores the impact of financial technology, demographics, and financial literacy on the economic decision-making of the productive age population in Surabaya. The study reveals that demographics (proxied by sex, income, and age)

do not significantly influence financial management behavior. However, both financial technology and financial literacy exhibit a positive and significant effect on financial management behavior. This study aligns with the broader theme of understanding how technological advancements and financial knowledge are crucial in shaping individuals' financial decisions. Suppose demographics have limited influence on financial management behavior, as Humaidi et al. (2020) suggested. In that case, including personalized emojis in mobile banking applications might serve as a universal element that appeals to diverse users. Personalized emojis have the potential to resonate with individuals across various demographic backgrounds, providing a familiar and relatable feature in the digital financial landscape.

Additionally, the positive impact of financial literacy on financial management behavior, as highlighted in Humaidi et al.'s study, suggests that users with higher financial literacy are more likely to make informed decisions (Humaidi et al., 2020). Including personalized emojis could enhance engagement within mobile banking applications, potentially facilitating the communication of financial information in a more accessible and engaging manner, thereby further improving financial literacy. Humaidi et al. study provides a foundation for understanding the roles of financial technology, demographics, and financial literacy in economic decision-making.

Furthermore, the study by Zhavoronok et al. (2022) focuses on the role of digital technologies in shaping households' financial behavior, especially in the context of the innovative economy. The research emphasizes the importance of understanding the interaction between families and financial institutions. It introduces indices for digitization and the transformation of economic behavior models, revealing regional variations in these indices within Ukraine. The study presents indices for digitization and the transformation of financial behavior models, showing regional variations within Ukraine. This finding implies that the impact of digital technologies on economic behavior is not uniform across different regions, highlighting the importance of context-specific considerations. Connecting Zhavoronok et al. (2022) research with the main topic of the impact of personalized emojis in mobile banking applications involves considering how regional variations in the digitization index and financial behavior models might influence the reception and effectiveness of customized features. Given the regional variations in digitization indices, personalized characteristics, such as emojis, could be tailored to address users' specific preferences and cultural nuances in different regions. Personalization might be crucial in ensuring the digital banking experience resonates with users across diverse contexts, contributing to a more inclusive and effective financial technology landscape (Zhavoronok et al., 2022).

Further, personalized emojis within mobile banking applications can serve as a tool to enhance user engagement, making the digital banking experience more appealing and user-friendly. In regions with varying levels of digitization, personalized features may contribute to increased adoption rates by creating a positive and relatable interaction between users and the technology. Zhavoronok et al.'s study and the main topic suggest that understanding regional variations in digitization and financial behavior models is crucial for designing compelling,

personalized features. By tailoring such features to users' specific needs and preferences in different regions, the impact on customer saving rates may be more pronounced.

Methodology

The research aims to investigate the impact of incorporating personalized emojis into mobile banking applications on users' saving habits. In response to the evolving financial sector and the widespread adoption of mobile banking, this study explores the potential of technology-driven nudges, specifically emojis, to positively influence users' financial decisions. Building on behavioral economics principles and the transformative role of technology, the research seeks to understand how personalized emojis, strategically integrated into mobile banking, can create emotional connections and encourage improved saving habits.

Literature Search and Selection Criteria

 Database Search

A meticulous literature search was undertaken across prominent academic databases, encompassing PubMed, JSTOR, and Google Scholar. Variations of search terms such as "emoji," "nudges," "mobile banking," and "saving rates" were employed to ensure a comprehensive exploration of relevant studies.

Inclusion Criteria

The studies selected for this meta-analysis adhered to stringent criteria to ensure their relevance, empirical focus, publication quality, and temporal relevance. Specifically, studies had to concentrate on the impact of visual interventions, exceptionally personalized emoji messages, within mobile banking applications. Only empirical studies with measurable outcomes related to saving rates, financial decisions, or behaviors were considered. Prioritization was given to peer-reviewed articles, conference papers, and reputable academic sources, and studies conducted within the past ten years were preferred to capture recent developments in mobile banking technologies and user behaviors. The table below displays the selected studies criteria of this research study

Selected Studies Criteria

Criteria	Description
Relevance	Studies must focus on the impact of visual interventions, particularly personalized emoji messages, within the context of mobile banking applications.
Empirical Focus	Only empirical studies with measurable outcomes related to saving rates, financial decisions, or behaviors were included.
Publication Quality	Peer-reviewed articles, conference papers, and reputable academic sources were prioritized

						to ensure the reliability and validity of the included studies.
Temporal Relevance						Studies conducted within the past ten years were prioritized to capture recent developments in mobile banking technologies and user behaviors.

Data Extraction

The data extraction method of this study is a systematic extraction, which is an organized process of gathering data from the selected studies. The goal is to acquire comprehensive and relevant information that will contribute to a thorough understanding of the impact of personalized emoji inclusion on customer saving rates. Data from the chosen studies were systematically extracted, encompassing essential study characteristics (authors, publication year, sample size), methodological details (study design, data collection methods), and key findings associated with the impact of personalized emoji inclusion on customer saving rates (see the table below).

Data Extraction and Coding

Study	Authors	Publication Year	Sample size	Study Design	Data collection methods	Key Findings
1	Bai et al.	2019	-	Systematic Review	Literature Review and Analysis	Emoji developed from emoticons and have both emotional and semantic functions.
2	Farida et al.	2021	112	Structural Equation Modeling (SEM)	Purposive Proportional Random Sampling	Financial literacy does not have a direct effect on financial behavior.
3	Gordon & Schindler-Ruwisch	2020	4208 students	Quasi-experimental design		- The beverage nudge significantly increased

						water consumption
4	Humaidi et al.	2020	180	Quantitative, Causal		Demographics (Sex, Income, Age) did not influence financial management behavior.
5	Lyons & Kass-Hanna	2022	-			- Introduction of behavioral economics impacts financial decision making.
6	Mozdeika	2023				
7	Oliver	2013				Application of behavioral economics to inform and justify regulations in the public sector.
8	Zhavoronok et al.	2022				modern digital technologies impacts the development of financial services, particularly households' financial behavior

Primary Outcome Measure

The meta-analysis primarily utilized effect size as the outcome measure, quantifying the strength and direction of the relationship between personalized emoji inclusion and customer

saving rates. Effect sizes, varying across studies, were contingent on the statistical metrics reported in each study, such as correlation coefficients, odds ratios, or mean differences.

Statistical Evaluation

Given the potential diversity in study designs and participant characteristics, heterogeneity among the selected studies was assessed through statistical methods. Subgroup analyses were executed to delve into potential sources of heterogeneity, such as variations in sample demographics, study settings, or methodologies.

Publication Bias Assessment

Publication bias was scrutinized through funnel plots and statistical tests, addressing potential biases arising from the selective publication of studies with significant findings.

Sensitivity Analyses

Sensitivity analyses were performed to assess the robustness of the meta-analysis results. This involved excluding studies individually and observing the impact on the overall effect size.

Ethical Considerations

Given the reliance on existing published studies, ethical considerations related to human subjects were not applicable. However, the research team ensured proper citation and acknowledgment of the original authors whose work contributed to the meta-analysis, upholding ethical standards in scholarly collaboration and recognition.

Results

The literature review in this study provides a comprehensive understanding of the diverse facets surrounding the impact of emojis in financial decision-making, incorporating insights from behavioral economics, emojis as nudges, and the influence of technology on economic behavior. Oliver's (2013) study introduces the concept of "budge," a noteworthy approach within behavioral economics that suggests the strategic application of behavioral insights in the public sector to influence policies. This introduces a novel perspective, proposing that behavioral economics can extend beyond the individual decision-maker to inform public policies. The idea of "budge" suggests a nuanced strategy for governments to navigate the complexities of general behavior without resorting to direct regulatory measures. The literature review further strengthens its foundation by incorporating Gordon & Schindler-Ruwisch's (2020) research, which delves explicitly into the effectiveness of nudges in the health sector. The study provides a tangible example of how subtle interventions, referred to as nudges, can play a pivotal role in guiding individuals toward healthier decisions.

By implementing straightforward instructions or cues in a college dining hall setting, the study illustrates that nudges can positively influence behavior without compromising individual freedom of choice. Rather than relying on strict regulations or mandates, the literature emphasizes the effectiveness of nudges – subtle, indirect interventions that nudge individuals toward making more positive decisions. This perspective challenges conventional regulatory approaches, opening avenues for more nuanced and psychologically informed strategies to influence behavior. By showcasing examples from public policy and health settings, the review

effectively sets the stage for subsequent sections to explore the application of similar principles in the financial realm, particularly concerning the integration of emojis as nudges in mobile banking applications. The emphasis on non-regulatory, psychologically informed approaches lays the groundwork for understanding how such interventions can influence financial decision-making.

Mozdeika's (2022) exploration of interpassivity introduces a theoretical framework that connects the practical applications of nudges and emojis in digital spaces. This framework challenges assumptions about user passivity in interactive digital environments, providing a lens to understand the delegation of emotional subject positions. This theoretical foundation adds depth to the discussion, suggesting that emojis, as a form of nudge, are not just passive symbols but active components that shape user experiences and decisions. Kass-Hanna and Lyons (2022) contribute significantly to the literature by delving into the psychological influences of emojis, particularly within financial decision-making. This study recognizes emojis as powerful communication tools and underscores their ability to convey a diverse range of emotions. The exploration of irony, passionate joking, and strategic ambiguity within far-right online subcultures highlight how emojis become integral in influencing financial choices. This deep dive into the psychological aspects of emoji usage prepares the groundwork for understanding how personalized emojis might impact users' emotional connections with their financial decisions.

The comprehensive understanding gained from this section forms the bedrock for investigating the incorporation of personalized emojis in mobile banking applications. By linking practical applications, theoretical frameworks, and psychological insights, the literature review successfully establishes emojis as more than just visual elements in communication. Instead, it positions them as potential nudges influencing financial decision-making's emotional and cognitive dimensions. As the review transitions toward investigating personalized emojis in mobile banking, it carries forward a nuanced understanding of emojis as active, influential components in the digital landscape. The groundwork laid in this section sets the stage for evaluating how personalized emojis might contribute to emotional connections between users and their financial decisions, ultimately impacting saving habits in the mobile banking realm.

Conclusion

In conclusion, this research paper navigates the unexplored terrain of leveraging personalized emojis as nudges within mobile banking applications to influence customer saving rates. The study emerged from a critical literature review encompassing diverse facets, including behavioral economics and nudges, the role of emojis in digital communication, and the influence of technology on financial behavior. Rooted in the insights of Oliver (2013) and Gordon & Schindler-Ruwisch (2020), the paper establishes the efficacy of non-regulatory approaches in shaping behavior, laying the groundwork for exploring a novel strategy within financial decision-making. The exploration of emojis as nudges, guided by Bai et al. (2019), Mozdeika (2022), and Kass-Hanna and Lyons (2022), presents a multifaceted understanding of these visual

elements. The theoretical framework of interpassivity and insights into psychological influences emphasize emojis as active components that shape user experiences. As the study transitions into investigating the impact of personalized emojis, it builds upon Farida et al.'s (2021), Humaidi et al.'s (2020), and Zhavoronok et al.'s (2022) research, revealing the intricate dynamics of financial technology, demographics, and regional variations in digitization. By connecting these diverse threads, the research paper sheds light on the potential of personalized emojis to enhance emotional connections between users and financial decisions. It underscores the need for context-specific considerations in implementing such interventions. The study contributes to the evolving discourse on the intersection of technology and economic behavior and provides financial institutions with a unique strategy to foster positive financial habits among users. Furthermore, it invites future research endeavors to delve deeper into the nuanced landscape of technology-driven interventions in the dynamic realm of personal finance.

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Arsenic Bioremediation with microbes based on Environments: a review By Lauren Her

1.Abstract

Arsenic, a heavy metal widespread in a variety of conditions, negatively impacts both human health and the environment. To reduce arsenic levels, bioremediation using microbes is a cost effective and sustainable method. This review will evaluate how to effectively implement bioremediation with different microbes to best suit various environments. Pseudomona genus, *Rhizobium* sp. NT-26, Skeletonema sp., *D. Palmitatis* with EDTA, *Herminiimonas arsenicoxydans,* and *Bacillus* sp. are of interest. A hypothesis that for bioremediating "hybrid" environments (environments with traits of multiple environments mixed together) with microbes, the microbe that could survive the environment with the harshest conditions among the environments in the mix being most suitable was made. Research incorporating other organisms, newer environments, and research in genetics will advance future studies.

2.Introduction

Arsenic (As) is a potential threat to both the environment and the organisms living in it. It has become a worldwide problem due to advances in industries, such as pharmaceutical and electronic industries (Chung et al., 2014). Being one of the World Health Organization determined carcinogenic chemicals, arsenic has impacted various environments, from groundwater to soil (WHO, 2022). Cases such as the contamination of San Joaquin valley made researchers more aware of the sources of contamination (Balazs et al*.,* 2012). Anthropogenic and natural sources such as industrial waste, mining residues, pesticides, or erosions cause chronic exposure to arsenic for humans, leading to health problems (Kapaj et al., 2006). Additionally, cases such as in Bangladesh, where arsenic contamination of a major groundwater source caused massive health issues, increased the awareness of the danger of arsenic contamination (Ahmad et al., 2018). Symptoms of Arsenic exposure develop quickly and depend on exposure time, with more critical impacts on the organs when ingested directly. Even a minimal amount of arsenic has potential to cause severe damage ((National Research Council (US) Subcommittee on Arsenic in Drinking Water, 1999). From light exposure symptoms, such as skin lesion, respiratory, or neurological complications, to chronic exposure symptoms, such as aggressive tumors or organ damage, symptoms can be detrimental to one's health and wellbeing (Abdul et al., 2015). As the estimated daily intake of inorganic arsenic in North America is 12–14 µg, it could be inferred that regardless of location, one should not take arsenic lightly (WHO, 2003). Inorganic arsenic species, considered especially toxic due to their strong bonds with organic materials, cause the symptoms described above. Possible of causing DNA breakdown, organic arsenic, although less of concern, still pose a threat to human health (Wang et al., 2009).

Current methods of arsenic removal, referred to as arsenic remediation, focus on either diluting the arsenic concentrations in their given environment to an accepted level, or using chemicals that could "wash" off the arsenic from the contaminated sites. While these methods

are effective and widespread, they tend to be costly and require expertise, limiting availability (Lim et al., 2014). Many methods are successful in lab environments, but are insufficient when directly used for contaminated environments, posing a major setback to these technologies. Due to the influence of a number of factors, such as pH, the oxidation state of arsenic, and redox potential, it is extremely difficult to eliminate arsenic on-site (Hassan et al., 2023). A method that addresses those setbacks is bioremediation. Bioremediation is the process of degrading the targeted contaminants through the use of living organisms, such as bacteria or fungi. Either used on sites (in situ) or off site in labs with controlled environments (ex situ), these methods are generally accepted socially for being cost effective, naturally sourced, and easily applicable without expertise (Vidali et al., 2001). Recently, microorganisms capable of As (III) oxidation have been used for the removal of other elements, including iron, suggesting the potential of bioremediating microbes (Bertin et al., 2022).

Microbes used in bioremediation are either collected from naturally occurring environments or human controlled environments. For low arsenic concentrations, naturally developed microbes are usually fitting. As they develop their capabilities specifically for the environment they were spawned in, they tend to thrive in environments similar to their origins. Modified for more challenging environments, engineered microbes are more suitable for areas with high arsenic concentrations. Strains that are genetically modified are likely to be applied, considering their high effectiveness (Lim et al., 2014). The major microbes that will be discussed in this review (including engineered microbes) are species from the Pseudomona genus, *Rhizobium* sp. NT-26, *Herminiimonas arsenicoxydans,* and *Bacillus* sp. While some are most apt for arsenic removal, others are most apt for the oxidation, converting arsenic to either a less harmful gaseous or ionic form. These microbes were chosen for their potential of having a high chance of being applied in situ, and for having abundant resources available (Anand et al., 2022).

This review suggests the most suitable microbes for different environments and conditions often found with arsenic contamination. Aquatic and terrestrial environments are of interest, along with conditions such as temperature and arsenic concentration. The specifics of each environment, such as the existence of other organisms like plants, or the salinity of aquatic environments, are also of interest. Limitations will be addressed through suggestions. There will be many opportunities for modifications to be made through future research pathways.

3.1 Physical Environments

Arsenic is present everywhere, from air to soil. Due to its persistence and high solubility, it is more prevalent in certain environments and poses a threat to its inhabitants. While arsenic contamination mainly occurs in water, soil environments could also get contaminated through geothermal activities or insecticides and pesticides (Chung et al., 2014).

Arsenic contamination has been found to be most impactful in Asian and Latin American water sources. Other developing countries that are outside of this continent are also greatly impacted (Rahaman et al., 2021). Human contamination generally occurs through the direct

ingestion of arsenic through water, or indirect ingestion through the accumulated arsenic in plants grown from contaminated soil and/or water. Other sources are more specific, such as sources such as air near arsenic contaminated environments or sources specific to rare events, such as volcanic eruptions (Chung et al., 2014). Four major sources, saline and non-saline environments, soil environments, and environments incorporating plants (relevant to arsenic contaminated agricultural land), will be of interest.

 3.1.A) Aqueous Environments

Saline Environments

For arsenic bioremediation of saline environments, only a few research cases exist. Most of these are done in oceans with high arsenic concentration levels, or by isolating certain strains ex situ. This is related to the relatively fewer numbers of contaminations in this type of environment. Compared to non-saline environments, saline environments generally display a low arsenic concentration (Ghosh et al., 2022). Micro or macro algae are more effective compared to other microbes. As primary producers, they tend to absorb or reduce arsenic more than higher members in a food chain. They absorb more arsenic as a result of their metabolism process, photosynthesis, which requires more water. Most algae flourish at low temperature seas(15~20°C) and at salinity between 10 and 35‰. The most active algae species is *Skeletonema* sp., which shows growth in a wider range of salinity and temperature. While none of the algae grow in temperatures under 0°C or aren't effective for low salinity conditions, there are cases where multiple species of algae were effective in arsenic bioremediation in temperatures above 0°C (Papry et al., 2019). According to the University of Hawaii at Manoa, the salinity of oceanic environments generally ranges from 33‰ to 38‰, with an average of 35‰ (Exploring Our Fluid Earth on Measuring Salinity, 2023). It is likely that *Skeletonema* sp. is most applicable to in situ environments with similar salinity to the ocean or the ocean itself. Other microalgae, such as brown algae isolate *Fucus spiralis* and *Ascophyllum nodosum*, absorb and accumulate arsenic in marine environments. These algae make inorganic arsenic more biodegradable and less harmful by converting them into organic forms. They also have potential of use in other saline environments with salinity similar to the ocean (Neff, 2009).

If considering isolating the contaminated water from sites and remediating the water separately, microbes other than algae are also viable. Marine microbes are a good option when considering candidate microbes. They are more arsenic resistant than non-marine strains, such as *E. coli, P. aeruginosa* and *B. subtilis*. One microbe to be considered is *Marinomonas communis*. *M. communis* is a non-engineered bacterium that accumulates arsenic and incorporates it into its cells. It shows effectiveness in a varying range of arsenic concentrations if incubated ex situ with a specific arsenic concentration. Because *M. communis* originates from the ocean, it can be used *in situ* as well (Takeuchi et al., 2007). Other bacteria to consider are *Alteromonas macleodii* and *Pseudovibrio ascidisceicola,* collected from the red sea sponge. If taken out ex situ, these two bacteria can reduce As (V) to As (III). To achieve optimal growth rates, they require a controlled environment due to their need of nutrients and need for lowered

salinity. However, the direct use of the red sea sponge species that the bacterium originated from *in situ* will be more ideal for higher effectiveness. These two bacteria, while frankly more suitable for non-saline environments, are included in this section for their have high potential of being used in saline environments as well in the future (Shoham et al., 2021).

Non-Saline Environments

Unlike saline environments, non-saline environments have vast data due to the abundance of contaminated sites. Rivers and lakes are the main sites found with contamination. While saline environments usually have a colossal scale of water involved, non-saline environments tend to be more at risk of getting high concentration arsenic contaminations because of smaller volume (Ghosh et al., 2022). One of the first bacteria that were found for arsenic bioremediation are arsenic oxidizers *Bacillus fusiformis* and *Bacillus cereus,* isolated from an underground water source in Taif city, Saudi Arabia. Able to remediate arsenic by absorbing it, they could remediate 0.127 mg of dry arsenic per gram. Used optimally in 30°C, the bacteria can lower concentrations to environmentally accepted concentrations in water in 12 hours (Mohamed et al., 2015). With other strains within the same *Bacillus* genus, such as *Bacillus sp*. KL1, KL4, and KL6, isolated from garbage leachate, they show the potential of use for this genus in arsenic bioremediation. Preferring slightly acidic to neutral pH conditions, these strains are also optimal for use *in situ* (Taran et al., 2019). Bacteria from this genus opened a path to arsenic bioremediation in non-saline aquatic environments along with other bacteria. Most are still suitable for use to this day as a remediator.

Bacteria available for arsenic bioremediation became more well known as data became more abundant. For instance, like the bacteria revealed through a case study on the high concentration of arsenic present in the Ganga River, India, AK1 and AK9 from the *Pseudomonas* genus. With most optimal conditions being 30°C, both strains have a high chance of survival both in situ and ex situ. They have high effectiveness, oxidizing arsenic up to 25% in 72 hours. They also have high tolerance for other heavy metals, such as lead or mercury. These strains are available for use in situ when other heavy metals are present, and are often used in environments with moderate temperatures (Satyapal et al., 2018). Collected similarly from arsenic contaminated aquatic sites, 3 gram-negative strains from Lahore and Kasur are able to remediate arsenic as well. They are more apt to resisting heavy metals compared to other strains collected from the same sites due to their two cell membranes. Although not able to oxidize As (III) to As (V), they remediate arsenic by accumulating a minimum of 39.16µg/L arsenic in 5 days. These strains have a maximum tolerance of arsenic at 50mM, and grow best at neutral pH, 37°C. They have a high optimal temperature, and are recommendable either ex situ or in situ environments with naturally high temperature (Iqtedar et al., 2019).

Some bacteria are optimally used with other strains or materials. *Bacillus* strains, for example, are optimized when used with specific strains. *Lysinibacillus sphaericus* EA1, *Bacillus fusiformis* EA2, and *Lysinibacillus* sp. EA3, when used together, enhances the effectiveness of the remediation process, boosting remediation rates to nearly 99%. Bacillus has significantly

higher rates compared to being used as the only strain in the same condition. Ironically having deterred rates in a mix of sole *Bacillus cereus* strains, the *Bacillus* strains show that optimal use are dependent on the choice of strains in the mixture (Mohamed et al., 2015). Another example would be *Herminiimonas arsenicoxydans*. Originating from an industrial water treatment facility, it can withstand high arsenic concentrations and can oxidize arsenic (III) to arsenic (V) (Bertin et al., 2022). Through a mechanism in its periplasm that converts arsenic into its less bioavailable form, arsenic (V), *H. arsenicoxydans* is one of the most suitable bacteria for this environment (Andres et al., 2016). *H. arsenicoxydans* can be incorporated with otbertinher bacteria that oxidize arsenic from arsenic(V) to arsenic (III). As often times arsenic remediating bacteria are unable to withstand extreme concentrations of either forms of arsenic, using multiple strains can balance the concentration of each type of arsenic and encourage more efficient and optimal remediation. Additionally, *H. arsenicoxydans* can be further utilized through activated carbon fiber biofilms. Activated carbon fiber biofilms, available to be spun out of recyclable carbonous fiber, catalyzes arsenic oxidation and allows the bacterium to form biofilms through their porous structure. With approximately an 50% increase in arsenic (III) oxidation compared to being used by itself, with carbon fibers, the bacteria could work especially well in contaminated sites involving arsenic (III) (Chen et al., 2022).

Acinetobacter gandensis and *Delftiatsuruhatensis*, discovered from industrial wastewater samples, also have similar traits with *H. arsenicoxydans.* Although not yet known for being used with other bacteria, these two strains, also tolerant of arsenic (III), can absorb approximately 30% of arsenic (III) present in 24 hours. Showing extreme improvement of arsenic (III) absorption when incorporated with chlorella, a type of single-celled algae, these strains can be further utilized in environments where chlorella can also be present. The co-use of algae with bacteria in aquatic environments has more potential of enhancing arsenic remediation based on this study. Several cases of algae species incorporation, such as red algae or chlorella improving heavy metal remediation, supports this claim (Zhao et al., 2023).

Bacillus firmus L-148, found from a soda lake in California is apt for remediation in a unique type of environment. It is hyper-tolerant of arsenic, tolerating both moderate to high levels of arsenic (III) and (V). Being able to oxidize 5 mM arsenic (III) in 9 hours and remediate extremely high concentrations of arsenic completely, it is extremely effective. As this bacterium is found thriving in soda lakes (lakes with a pH between 9 to 12) and has a higher growth rate when iron is also present, it can be used especially for environments involving high pH (Bagade et al., 2020).

In addition, *Alteromonas macleodii and Pseudovibrio ascidisceicola,* discussed previously from the saline environments section, are also of interest for non-saline environments. These strains could be used *ex situ* in non-saline environments. With *Pseudovibrio ascidisceicola* having unaffected growth rates in high arsenic concentration environments, these strains will show effectiveness when considering ex situ remediations for this environment (Shoham et al., 2021).

3.1.B) Terrestrial Environments–Soil Environments

Soil environments, although found less abundantly than aquatic environments, are still oftentimes found next to arsenic contaminated water sources or anthropogenic arsenic sources. Remediation of heavy metals in soil environments are more difficult because they typically form stable solid compounds (Wróbel et al., 2023). Microbes that use arsenic (V) oxidation as their remediation method are ideal in soil. As it makes arsenic more mobile, it eases the extraction of oxidized arsenic (Wang et al., 2009). Remediation rates of the bacteria used depend on specific soil conditions. Unlike a body of water, soil conditions can differ for each portion. Extra care is needed when selecting a bacterium for soil (Vaxevanidou et al., 2008). *Bacillus*, mentioned in the previous section, has extremely high absorption rates of heavy metals in soil as well. With high tolerance rates of a variety of factors, such as temperature, drought, and radiation, and the ability to remediate other harmful metals, it is considered one of the most viable bacteria for this environment. Commonly found in soil, species from the *Bacillus* genus containing the genes *arsA*, *arsB*, *arsC*, *arsD*, and *arsR* are the best fit for in situ remediation (Wróbel et al., 2023). Methods such as bioaccumulation can be considered. However, the difficulty of separating microbes from soil after remediation is a factor to be acknowledged. Further advances in technology related to soil-microbe separation would enhance the capability of microbes such as *Bacillus* that use bioaccumulation (Wang et al., 2009).

From 10 different strains of arsenic remediating bacteria isolated from arsenic contaminated soil in Chakdah, India, RJB-1, RJB-2, RJB-3, RJB-A and RJB-C are apt for use. Belonging to γ-*proteobacteria,* these bacteria show high remediation rates for arsenic (III) and arsenic (V). They either form long chains or reduce in size when exposed to either form of arsenic due to the stress, and remediate arsenic by accumulating it. After absorbing them as amino groups in their cell walls, the bacteria ultimately reduce or oxidate the arsenic ions. RJB-1, RJB-2, RJB-3, and RJB-A are significant for their high arsenic resistance and ability to produce siderophores. Siderophores, a type of molecule that mobilizes heavy metals (including arsenic) by converting them from a solid to aqueous phase, are extremely helpful for arsenic remediation. It is a suitable substance as it increases the amount of arsenic each bacterial cell can take through intracellular absorption. These strains, resistant to multiple types of heavy metals with a MIC range of 10-30mM for each, are suitable for in situ use. Since the bacteria used does not release most of the oxidized arsenic after processing them, with technology to remove bacteria being available, it could be further considered for in situ (Banerjee et al., 2011).

Genetically modified bacteria are also of interest in this environment. *Pseudomonas putida* with ArsM, a gene specific to arsenic (III) methylation, is one of them. With slight arsenic tolerance before being modified, this bacterium shows approximately 4~5 times more tolerance after being modified. While it shows lower rates of remediation than *E.coli* with the same ArsM gene, the overproduction of heterologous proteins in *E.Coli* are more harmful than beneficial, proving *P. putida* to be more suitable for in situ environments (Chen et al., 2013).

Especially in delicate soil environments, incorporating conventional methods such as use of chemicals with bioremediation is also considerable. *Desulfuromonas palmitatis*, an anaerobic

microorganism, is a bacterium that requires a specific compound to be used with it to be effective. Being anaerobic, this bacterium is mainly suitable for ex situ environments and requires additional nutrients and carbon. While both EDTA (Ethylenediaminetetraacetic acid) and *D. Palmitatis* are considered ineffective when used by themselves, when used together, their remediation rates go up to 70%. Through the dissolution of Fe (III) oxides, EDTA and *D. Palmitatis* work to release arsenic. Addition of another compound, NaHCO3, further enhances the effectiveness up to 90%. While EDTA is not highly biodegradable, it is known to decompose with the use of additional strains. Showing noticeably high removal of 95% for lead and up to 60% of iron, this mix is suitable for soil contaminated with multiple types of heavy metal (Vaxevanidou et al., 2008). Addition of chemical nutrients are considerable for all types of bacteria regardless of in situ or ex situ. Carbon sources are known to enhance the rate and effectiveness in general. For bioremediating bacteria with consideration of the environment, appropriate amounts of the chemicals can be effective and cost-worthy.

Soil Environments with plants

When plants are present in soil environments, they are an additional factor that impacts the microbes used for bioremediation. Depending on the type of plant, microbes used can either assist growth of the plant in the contaminated site or be used together with hyperaccumulating plants (plants that could accumulate high levels of heavy metal) (Wróbel et al., 2023). Microbes are also known to assist plants' adaptation of arsenic contaminated environments both in situ and ex situ conditions (Ma et al., 2011). Arsenic entry from soil to humans typically occurs from humans ingesting agricultural crops grown in arsenic contaminated soil. Therefore, considering human health, there is a need to remediate soil. Alterations in the plant microbiomes could build resistance for all plants, including agricultural plants. However, considering the delicate plant biomes with complicated soil biomes simultaneously is extremely difficult. Studies should be carried out considering various stress factors for both biomes especially for in situ environments. The most primary thing to consider is the plant species. Results vary drastically and depend on the host plant used for research (Ali et al., 2022). Although it may be nearly impossible to match each bacterium to a plant, this section will suggest the most alterable microbes and microbes specific to certain plants used in agriculture.

Studies done on the use of plants and the microbe *Bacillus* are mostly done in controlled situations. They suggest that for being utilized in ex situ with plant life, more in situ studies are ideal for *Bacillus* (Wróbel et al., 2023). A certain few species of *Bacillus*, capable of assisting bioaccumulation of heavy metals in soil with plants in situ, may pave the way. *Bacillus aryabhattai*, found from a soil sample in Durgapur, India is one of the few. Showing higher growth rates when in the presence of As (V) and slower rates in As (III), it removes 41% of As (V) and 26% of As (III) between 24 to 36 hours. Since As (V) reduces phosphorus available to plants and deter plant growth (which is critical for agriculture), the bacterium's ability to remediate As (V) is valuable. *B. aryabhattai* has also shown growth promotion of rice seedlings

by reducing damage through ethylene production. One of the unique microbes suitable for in situ use, it is suitable for arsenic contaminated agricultural sites (Ghosh et al., 2018).

Pseudomonas sp. ASR1, gained from an agricultural soil source in Taiwan, is also of interest for in situ remediation. It could remediate arsenic (III) while boosting plant growth through traits such as phosphate solubilization or siderophore formation. This bacterium can grow in a notably wide range of pH and temperature through a detoxification mechanism. However, it should be noted that it is unable to remediate arsenic while having arsenic (III) as the sole electron donor when being grown initially for remediating soil with plants ex situ (Das et al., 2014). Also found in other strains from Pseudomonas, it produces IAA, an acid that promotes growth of plants. This genus has bioremediation potential with plants (Ma et al., 2011). *Pseudomonas stutzeri* and *Pseudomonas putida,* separate from *Pseudomonas* sp. ASR1, has similar traits to *Pseudomonas* sp. ASR1. While ASR1 is the most efficient microbe when considering remediation rates and plant growth promotion, the other pseudomonas microbes still have the same abilities to a lesser degree (Das et al., 2014). In some situ studies, *Pseudomonas* were only found in agricultural plant rhizospheres (Sultana et al., 2023), indicating that in some cases, this bacterium may not work without agricultural plants. Therefore, it is especially considerable for agricultural soil with plants.

For arsenic remediation through arsenic absorption into plants, especially when the plants aren't agricultural plants, *Azotobacter* and *Bacillus* can be considered. These bacteria prevent excess amounts of arsenic from being absorbed by plants. They absorb a portion of arsenic to their walls, and form a barrier to prevent arsenic from being overly absorbed in high concentrations. They are, however, unsuitable for higher pH. Because arsenic becomes more immobile in high pH levels, the microbes increase the plants' absorbance of arsenic. *Azotobacter* and *Bacillus* are therefore more preferable for in situ environments near contamination sources. Additionally, they are more apt to be a supplementary microbe, as they are further capable of mobilization and immobilization of arsenic in a narrow range of pH than direct remediation (Belogolova et al., 2015).

Either usable with plants in situ or just in soil near plants, *Rhizobium leguminosarum* bv. *Trifolii* modified with an algal gene, *CrarsM,* is of interest. Arsenic bioremediation that uses both plants and microbes tends to be limited in the rhizosphere of plants. Therefore, the use of engineered microbes that may exceed the limits, like *R. leguminosarum* are not to be ignored. This bacterium alters most of the inorganic arsenic present, mainly As (III), into further methylated forms of arsenic. Most inorganic arsenic is converted to DMAs (V) (dimethylarsenate), while a portion is converted to MAs(V) and TMAs(V)O (methylarsenate and trimethylarsine oxide). *R. leguminosarum* is able to convert a small portion of arsenic into volatile forms. R. *leguminosarum* likely shows similar arsenic volatilization capabilities to *Chlamydomonas reinhardtii,* the origin of the CrasM genes. Retaining the bacterium's original ability to alter nitrogen concentrations, the bacterium decreases arsenic concentration in the roots and a slightly increases arsenic in the nodules of the plant (Zhang et al., 2017).

Also from the Rhizobium genus, *Rhizobium* NT-26, an arsenic oxidizer, should not be ignored. It grows chemolithoautotrophically (gather their carbon from CO2 nearby) by using the remediation reaction as a source of energy. It possibly uses arsenic as an electron donor. In the presence of small organic matter, such as yeast, it is able to decrease its doubling time significantly (up to approximately three times) and is able to remediate arsenic with higher efficiency. Showing the high effectiveness in pH 5.5, it does require a minimum of 1 week and an addition of 2mg of magnesium or calcium for its significance to show in some experiments (Santini et al., 2000). Moreover, while *R*. NT-26 doesn't perform direct symbiosis such as plant nodulation with plants, it both directly and indirectly benefits plant growth by generating plant growth regulators. *R*. NT-26 reduces heavy metal concentrations through providing/reducing nutrients such as nitrogen or phosphorus, and competes with plant pathogens. It also tolerates concentrations greater than 0.5M (Andres et al., 2013). It should be noted that organic matter such as yeast deters *R*. NT-26 when it is grown together with the bacterium when initially cultivating the strain for use. Because the bacterium uses yeast as another source of energy if done, it utilizes arsenic less (Santini et al., 2000). This bacterium is more suitable for both in situ and ex situ environments, but is more suitable for ex situ as it may require a one-week incubation period.

As a separate note, engineering plants with the genes of arsenic resistant or remediating bacteria is also an option. There are several cases where plants, such as *Arabidopsis thaliana*, gained higher arsenic resistance and accumulation rates after being altered with a bacterial gene. A case that was successful to transfer arsM genes from the bacterium *Rhodopseudomonas palustris* to rice also exists. While the alteration had only a miniscule effect, the rice did methylate arsenic. Being able to volatilize arsenic as well, these cases show potential of using microbe genes on plants (Zhang et al., 2017).

Prospering in both agricultural and conventional plants, *Exiguobacterium,* discovered from arsenic contaminated soil is notable. With its sample host plant *Vigna radiata,* a type of bean plant, it was able to remove approximately 99% of As (V) and 90% of As (III) in a week. It has fast remediation rates and is slightly more efficient in removing As (V). Unless in extremely high arsenic concentrations, it shows no difference in plant growth. When applied, *Exiguobacterium* colonizes in the rhizosphere soil, increasing chlorophyll concentrations of the plant and increasing solubilization of phosphate. Due to the bacteria absorbing portions of arsenic, it simultaneously decreases arsenic accumulation by 5 folds in the roots and 3 folds of shoots in plants (Pandey et al., 2016).

Similarly prospering the most in both agricultural and conventional plants, *Sphingomonadaceae* has similar properties to *Exiguobacterium*. Some differences would be that *Sphingomonadaceae* could prosper in bulk soil that does not include plants as well and is tolerant of 7 different heavy metals. By solubilizing phosphate and producing ammonia, it also has high levels of catalyzation and benefits plants to a certain degree. This bacterium, however, while showing tolerance for arsenic, is not as efficient in remediation. Although capable, it should be considered less (Sultana et al., 2023).

Brevibacillus sp. KUMAs2, a bacterium with high resistance to arsenic and availability to remediate arsenic, due to its rather low remediation rate (up to 40%), is shortly mentioned. If considered for use, it could be used for agricultural grounds as it showed abilities to promote plant growth (Mallick et al., 2014).

3.2 Conditions/Conditional Environments

This rather brief section will go through the "conditional" environments. These are factors that are not to be overlooked, as each microbe has a different level of tolerance for conditions of their physical environment. In some cases, they also have specific factors, such as presence of specific ions or moisture levels. Oftentimes, adjustments on sites can be made for microbes. Considering that, conditions that will be described are not constants, but rather, variables. A strain from the B*acillus* genus, *B. cereus*, for example, has a arsenic concentration limit of 15 mg/L (Mohamed et al., 2015). If levels of arsenic are adjusted beforehand, the remediation process would be much more effective. In other occasions, adjustments can be made to the microbes when cultivating them in the first place. Adjustments can be made by either changing surface area of contact (such as by using biofilms) or altering genes of the microbes to be more effective as in the many cases from the previous section. Efficiency of bioremediation differs by its pretreatment (Kapahi et al., 2019). While availability to adjust environments differ depending on ethics, funding, and other anthropogenic impacts that may occur on site, it is an option that would likely display better results.

This section will go through the general conditions preferred by arsenic remediating (or heavy metal remediating) microbes, and if data is available, describe specific conditions that the key microbes in this paper prefer. Other conditions such as time, genes, pH, differing relatively more than concentration and time, will be brushed through.

3.2.A) Concentration

Even for species of the same genus, such as *Bacillus*, different tolerance levels for concentration exist. A study shows that in the exact same conditions, *Bacillus* KL6 tolerated a maximum 90ppm of arsenic, while *Bacillus* KL1 tolerated 225ppm, showing a difference of more than twice the maximum tolerable arsenic concentration of KL6. *Bacillus* is one example having different maximum concentrations despite having no difference in external factors. The same strains also show different concentrations of arsenic for their optimal remediation conditions, suggesting that different concentration preferences for maximum and optimal remediation exist even with the same genus and conditions (Taran et al., 2019).

The pH levels, also known as the concentration of hydrogen ions, are equally important. It is known that for the majority of arsenic remediating bacteria, the most optimal range of pH is between 5 to 7. While it shouldn't be considered as a rule of thumb, it is still considerable when setting up initial conditions for microbes. *Bacillus* KL6 and two other strains from the study mentioned above works best at pH 5 as well (Taran et al., 2019), while Pseudomonas AK1 and AK9, mentioned in the non-saline environments, grew between pH 6 to 9. Although some

environments, such as calcareous soils, have a buffering effect and may be tedious to alter, the alteration of pH is helpful in some cases (Vaxevanidou et al., 2008). The fact that pH is influential in the general chemistry of the environment that both arsenic and the microbes are present should never be forgotten. As pH impacts a variety of factors by causing reactions including redox or hydrolysis, condition changes by this factor is critical to success of remediation (Kapahi et al., 2019). Alteration of the pH itself when remediation occurs is not rare as cases, such as *D.Palmitatis* increasing pH values in the remediation process (Vaxevanidou et al., 2008). Therefore, determining whether to occasionally alter the pH to the target value, or to not make changes after the initial alteration should be done as well.

3.2.B) Temperature

Temperature and concentration both influence each other, and oftentimes cause huge changes if altered (Far et al., 2023).

Temperature causes difference in bioremediation effectiveness for strains such as B*acillus* KL1 when altered. In KL1's case, the difference was up to 77% (Taran et al., 2019). Therefore, when considering to alter temperature, impacts on concentrations should be considered. In a study of sedimentary microbes in a subarctic lake with low temperature, specific microbes mobilized arsenic better and preferred low temperature levels (Miller et al., 2022). In another study, specific microbes showed reduced efficiency in high temperatures (up to 40°C). The bacteria for this study were best grown at temperatures hotter than room temperature (between 30 to 35°C) (Taran et al., 2019).

Likewise, the temperature preference for microbes differs (in some cases, radically). It is important to find a temperature at which the majority of the microbes are able to remediate arsenic and survive in consensus, with the right amount of incubation time when in ex situ. A handful of studies suggest that oftentimes, overly incubating cultures may actually deter the effectiveness of microbes on arsenic. Microbes such as the previously mentioned *Rhizobium* sp. NT-26, which showed slower growth after 36 hours but still had no decreasing effectiveness, suggests that exceptions exist (Santini et al., 2000). However, generally incubating cultures for too long is not ideal.

3.2.C) Summary/Results

Arsenic, a carcinogenic chemical that has a link to health issues from skin leisure to tumors even with a minimal amount, is a threat to the environment and human health. Harmful either in inorganic or organic forms, it is essential to be removed, or remediated. While current methods of arsenic remediation dilute arsenic to less harmful concentrations or use chemicals, they tend to be costly and most of the time are not applicable in situ. Therefore, bioremediation of arsenic using microbes which are cost effective, considered sustainable and applicable in situ and ex situ, is ideal.

Saline aquatic environments, majorly the ocean, has low risk of contamination due to its vast volume. However, if needed, micro or macro algae such as *M. communis* is applicable. It is

ideal for more research to be done for saline aquatic environments, as this environment has relatively less research done on it. Non-saline aquatic environments, such as lakes and rivers, are more commonly found with arsenic contamination. For them, *H. arsenicoxydans*, *Bacillus fusiformis* and *cereus, Lysinibacillus* sp. are considerable. With abundant data, this environment has a variety of strains to be used both in situ and ex situ.

Soil environments, typically more difficult to bioremediate due to the presence of other heavy metal and matter, are quite abundantly found with contamination. Unlike liquid solution environments that are more unfixed, terrestrial environments are more immobile and irregular. Microbes that use arsenic (V) oxidation that makes arsenic more mobile are considered more ideal for soil. Microbes such as species from the *Bacillus* genus that have specific soil remediating genes, genetically modified *Pseudomonas putida*, and to *D. Palmitatis* incorporated with EDTA are recommendable for soil. And for soil with plants, such as agricultural crops or simply plant life either capable of arsenic accumulation (or not) present, microbes that could either remediate arsenic, assist arsenic accumulation in plants, or/and boost plant growth are recommended. *Pseudomonas* sp. ASR1, *Bacillus*, *Rhizobium leguminosarum,* modified with an algal genes, *Rhizobium* NT-26, and *Exiguobacterium* are suggested.

Factors that may be altered such as concentration of arsenic, pH, temperature, and time are essential to be considered. As different factors impact each other, such as concentration and temperature, more insight into the altered conditions is needed. Microbes have different tolerance for all factors, even after being grown in the same conditions or even after being from the same genus. Therefore, choosing the optimal conditions for all microbes used for remediation, especially when using multiple types of microbes, are recommended. Additionally, for alteration of conditions, changing the conditions of the environment before the microbes are used, or growing microbes initially with altered conditions or genes are helpful for greater remediation

Choosing a microbe by environmental conditions

IS THE MAIN REMEDIAITON SITE ON LAND/SOIL?
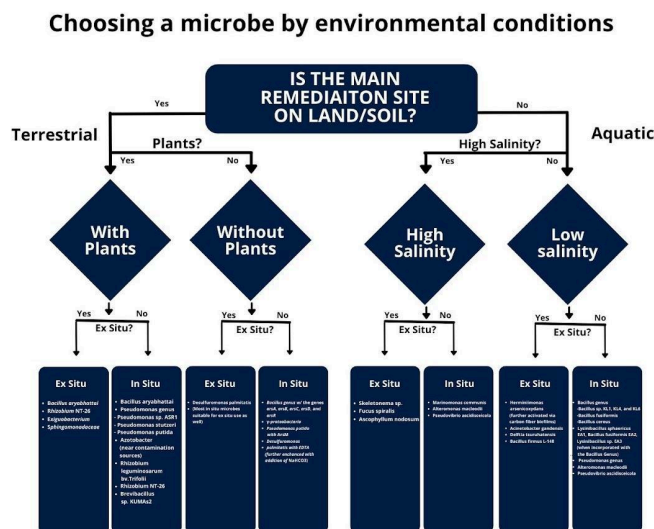
effects.

Figure 1: A flow chart summarizing which microbes to choose by environmental conditions. Original template credits to © Canva.com. Modified to fit needs by Lauren Her.

4. Limitations and future directions

Although the common environments found with arsenic contamination were looked into, classification of the environments were rather broad. Environments that are rarely contaminated, but still can be found with contamination may need further research, such as aerial environments (that could be contaminated via arsenic attached to particles in the air) or environments that are in between, such as swamps or marshes. While research for some of these environments does exist, the majority of the existing research does not provide enough information or is not significant enough for use. Research in those environments may accelerate research in other, more common environments. Different classifications of aquatic environments other than salinity would be beneficial to the study of arsenic remediation. Hinted from the aquatic environment section, salinity may be a minor concern to microbes that live in extreme environments with either high or low pH and temperature. There are certainly limitations to determining which microbes would be the best to be used for it. Therefore, more clear methods to evaluate arsenic remediating microbes that could be agreed with as many microbiologists as possible would be the best for both saving time and funding that goes in for research.

Additionally, more research on general conditions for arsenic remediating bacteria may be helpful. As mentioned before, the spectrum of bacteria is very broad, with a broader tolerance for various conditions. Determining the suitable conditions for at least the most commonly used general would be time saving and beneficial. More factors may be looked into in the future. There are other factors than pH, concentration, or time such as the species' specific genes, solubility, the harmony of arsenic itself with other chemicals, and addition of chemicals with relatively less-known effects, such as other heavy metals. Some genes, such as arsA, arsB, arsC, arsD, and arsR or CarsM genes being well known compared to other genes related to remediation already suggests that the study of bacterial genetics involved in arsenic bioremediation will be essential.

In the future application of the microbes, the long term and short-term impacts on the environment should be considered. Applying microbes, especially bacterium, although having a lesser concern of harming the environment than conventional methods, can cause unpleasant odor or have impacts caused by the materials used for the remediation process. Bioremediation generally has a reputation of being the "better" choice for it being sustainable and more cost effective already, but it may require methods to make the public to be more accepting of this branch of remediation. For application, especially in situ, barriers such as opposition from nearby residents or regulation due to the lack of knowledge of the public could be a drawback.

5. Conclusions

From the assorted microbes, one or two of the microbes for each environment can be selected as the most ideal. Microbes with more adaptability in situ are optimal since microbes being applied in situ would be more cost efficient and accessible. The best microbe for in situ remediation in aquatic environments is *Skeletonema* sp. for saline environments and *Herminiimonas arsenicoxydans* for non-saline environments. The most apt microbes for in situ

terrestrial environments are either γ-*proteobacteria* for environments that have strict regulations on use of inorganic chemicals, and *D. Palmitatis* with EDTA if there are no limits for using EDTA with the microbe. With terrestrial but with plants, the *Pseudomonas* sp. is emphasized.

Environments that didn't fit into any of the categories from section 3, especially for those that are a mix of two environments such as wetlands, or aquatic environments that involve plants, bacteria that survive the harsher environment of either of the two will adapt to the other. As a general trend in this review, microbes that were able to withstand environments with factors such as salinity or the presence of heavy metals that are threats to them were able to survive in environments that didn't have those threats.

And for future research in arsenic bioremediation, search for arsenic remediating microbes should be done not only at arsenic contaminated sites, but other sites with the potential of having microbes as well. There were multiple cases, some of them mentioned in the previous sections, that the bacterium originated from non-arsenic contaminated sites. Even without genetic modification, some showed moderate arsenic remediating (and tolerating) skills. The genetics of microbes seemingly unrelated to arsenic contaminated sites or being exposed to high concentrations of arsenic showing remediation traits are to be looked into. As bioremediation for soil including plants was effective, the use of other living organisms beyond plants, such as fungi, is ideal for future research. Fungi is extremely variable and has high potential of being used with bioremediating microbes or even individually.

Acknowledgements

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Stroke of Luck?: Investigating cellular hemin uptake mechanisms in hemorrhagic strokes
By Tanya Siddiqui and Arianna Broad

Abstract

Hemin oxidizes from heme in the presence of a hemorrhagic stroke and slowly internalizes into cells through multiple methods, including the hemin-hemopexin complex through a lipoprotein receptor, the implementation of the heme carrier protein, and the natural peroxidative ability of hemin. It is unknown whether these three internalization methods have the ability to work in sync with one another or if they work one after the other. The hemin-hemopexin complex can be internalized into the cell using the low density lipoprotein receptor 1, as the two are known to have a high affinity to one another. The heme carrier protein 1 has some connection to the protoporphyrin ring that is present in hemin, and is speculated to be an internalization protein. The ability of hemin to peroxidize lipids can weaken the structure of the cell membrane and render it susceptible to its internalization.

Introduction

Stroke is a major cause of death and disability worldwide. It has an annual mortality rate of 5.5 million and a vicious morbidity, resulting in about 50% of all survivors being chronically disabled (Donkor 2018). Strokes can be categorized into two types: ischemic, which constitutes for 87% of all strokes, and hemorrhagic strokes, which accounts for 13% (Virani et al. 2020). Hemorrhagic stroke occurs by the rupture of a cerebral artery, resulting in the accumulation or pooling of blood, or hematoma, in the extra cellular space of neurons (Robinson et al. 2009). Whereas in ischemic stroke a blood clot inhibits blood flow to the brain. While hemorrhagic stroke is less common than ischemic stroke, it is more deadly. Intracerebral hemorrhage constitutes 10-20% of all strokes and is a highly morbid pathology, with only 12-39% of people getting their functional independence back after a year (van Asch et al. 2010). Treatments for hemorrhagic stroke are very limited and research has shown that the only viable treatment option for the best survival and recovery outcomes is immediate surgery to prevent further primary tissue damage, which refers to the effects of physical compression and pressure of neural tissue due to the presence of the hematoma (Aronowski and Zhao 2011). However, secondary damage can ensue in the following days and weeks, which can arguably be more detrimental than the initial primary damage. Secondary damage refers to the toxic effects of hemin and reactive oxygen species (ROS) to the cells proximal to the hematoma (Robinson et al. 2009). A hematoma consists of blood that seeps into every nook and cranny between neuronal cells, forming a mass in the brain (Dang et al. 2011; Stokum et al. 2021). The blood that comprises the hematoma includes lysed red blood cells (RBCs) called hemolysate, which results in the accumulation of cellular debris and the spilling of their contents including oxygen and heme. The mechanism of oxygen and heme dissociation from the globin protein in hemoglobin (the protein responsible for carrying oxygen through the bloodstream) results in the formation of ROS. Additionally, the increased energy requirement to clear extracellular debris accumulation places

more undo stress on the proximal neurons. Therefore, blood accumulation in the neuronal extracellular space then induces the oxidative stress response in a rapid manner (Jelinek et al. 2021).

Hemolysate is toxic not only due to the ROS causing neuroinflammation and oxidative stress, but also due to the formation of hemin from heme (Jaremko et al. 2010). Heme is a small porphyrin molecule that coordinates the binding of iron and oxygen to the globin protein. When heme is bound to globin, the iron it coordinates is in the +2 oxidation state (Fe^{2+}), rendering it non-toxic whether it is also bound to oxygen or not as the electrons are shared in a covalent bond. However, once heme dissociates from globin it loses a lone electron to physiological oxygen (O_2) creating a reactive oxygen species such as hydrogen peroxide and hydroxyl radicals, while also resulting in the further oxidation of heme to the +3 oxidation state (Fe^{3+}), a compound referred to as hemin (Ray et al. 2012). This breakdown of hemoglobin and generation of ROS not only causes the oxidation of cellular lipids, proteins, and DNA, which can lead to eventual cell death, but also creates byproducts from the degradation of hemin, via heme oxygenase (HO1) action, such as iron, carbon monoxide, and biliverdin, which can all be toxic in high concentrations (i.e., when the hemin cellular uptake mechanism is overloaded from a hemorrhagic stroke) (Sinha et al. 2013; Dang eat al. 2011). Cell death in the brain due to hemin is able to cause permanent and irreversible damage. To illustrate, if 2.5mL of hemoglobin is present in blood, when broken down it will make 10mL of hemin, where it is also known that anywhere between 3mL to 30mL of hemin can kill 60-70% of neurons within 14-40 hours of the stroke (Chen et al. 2004; Regan et al. 2002). Once hemin is cellularly uptaken through non-canonical recycling mechanisms, oxidation of lipids, DNA, and cellular proteins, which will alter their function, is imminent.

The uptake of hemin into cells is known to facilitate cell death, but the mechanisms of cellular hemin uptake are not fully understood. Proteins known as hemopexin, through its receptor, the low density lipoprotein 1 (LRP1), and the heme carrier protein 1 (HCP1), are both known to facilitate hemin uptake. Lipid peroxidation is also a putative hemin uptake mechanism, barring the knowledge that hemin is a hydrophobic molecule that has the ability to passively enter the cell membrane under certain conditions (Belcher et al. 2010). Therefore, the purpose and scope of this review will be focusing on understanding the known hemin cellular uptake mechanisms and speculating how these mechanisms are interconnected and if they play a compensatory role in overcoming the overwhelming challenge posed to cells undergoing hemorrhagic stroke.

Hemin Cellular Uptake Mechanism One: *Hemin-Hemopexin Complex via the Low Density Lipoprotein Receptor 1 (LRP1)*

Hemopexin is a protein present in cerebrospinal fluid that dampens effects of toxic hemin released in hemolytic conditions. Hemopexin is most abundantly expressed in neuronal cell types, and expression of hemopexin is relatively high compared to other neuronal protein concentrations (Stibler 1978). It is proposed to lessen the toxic effects of hemin once

internalized into the cell, however the precise mechanism of this has yet to be elucidated. It is speculated that the mechanism relies on the abundant presence of histidine binding between heme/hemin and hemopexin. Surface plasmon resonance (SPR) studies have recently found that heme/hemin binds to hemopexin at an extremely high affinity ratio of 1:1, respectively, although another study claims that the affinity is even higher, at a heme-hemopexin ratio to be 2:1 (Detzel et al. 2020; Lechuga et al. 2022). Serine and glycine residues were also found to be important in interactions between hemin and hemopexin. Interestingly, another study found that protoporphyrin IX (a fluorescent analog of hemin) binds to the low density lipoprotein strongly, as it emitted a high wavelength upon binding (Camejo et al. 1998).

Human hemopexin is known to be able to interact with the low density lipoprotein receptor 1 (LRP1) through its ability to peroxidate lipids. LRP1 is a transmembrane receptor linked to intracellularly intake over 40 different ligands (Grosso et al. 2019). Furthermore, levels of LRP1 and hemopexin were found to be elevated in murine brain tissues 2 weeks post-surgery to stop a intracerebral hemorrhage (Wang et al. 2017). This same study also found that when human LRP1 was heterologously injected into the hematoma site, hematoma clearance and recovery outcomes improved. This is likely due to additional LRP1 allowing an increase in hemopexin endocytosis, allowing more heme to be scavenged and neutralized, lessening the oxidative stress on the hematoma-proximal neurons. To test this, Hvidberg et al. (2005) utilized SPR on hemopexin-LRP1 and heme-LRP1. They found that hemopexin and LRP1 bind strongly, whereas no binding was detected between heme and LRP1, suggesting that hemopexin acts as the adaptor protein to initiate the internalization of hemin via LRP1. The abundant co-expression and co-dependency of LRP1 and hemopexin synergistically protects the neural tissue against hemin toxicity (Hvidberg et al. 2005). To further elucidate this mechanism, it was found that an hour after the introduction of the hemin-hemopexin complex to primate cells, which are known to express LRP1, degradation products were present indicating that the hemin was endocytosed, likely mediated by LRP1. Expanding on Hvidberg et al. (2005), it was recently demonstrated that introduction of hemin into transformed human erythroblasts induces increased expression of hemopexin and LRP1, implying a ligand-receptor expression regulation cycle (Grosso et al. 2019).

Hemopexin, being abundant in the brain, is a ligand that binds to hemin with a strong affinity, with traces of binding on histidine, serine, and glycine, creating the hemin-hemopexin complex. A hemin derivative with common properties had a significant bond to the low density lipoprotein, suggesting that hemin would also have a strong bond with LRP1 for endocytosis. Numerous studies have suggested that an increase of hemin leads to an increase of the presence of LRP1 and hemopexin. It has also been found that hemopexin must be present for heme to be internalized, leading to the formation of degradation products within the cell. The co-dependency of these speculates that LRP1 is responsible for the recognition of hemopexin and endocytosis of the complex.

Hemin Cellular Uptake Mechanism Two: *Heme Carrier Protein 1 (HCP1)*

Heme Carrier Protein 1 (HCP1) is a transport protein that is said to facilitate heme uptake in astrocytes, a neuronal cell type. However, it is also known as the proton-coupled folate transporter, implying that HCP1 is multi-functional (Li et al. 2017). Unlike the first hemin uptake mechanism described, with HCP1, hemin doesn't need to form a complex with any other protein in order to be internalized by HCP1. It is currently thought that the specificity of HCP1 is correlated to the protoporphyrin ring and not the metal itself, as zinc protoporphyrin (ZP) is also able to be internalized using the transporter (Dang et al. 2011). Presence of HCP1 in the human central nervous system is not confirmed, but it is abundantly found in liver and kidney cells (Shayeghi et al. 2005). However, Dang et al. (2011) found that HCP1 mRNA was abundantly expressed in rat astrocyte cultures and HCP1 antibodies were also detected. They also demonstrated that HCP1 protein concentration decreases after hemin exposure. To further explore if hemin utilizes HCP1 to be internalized, they conducted an experiment to determine if ZP also has the ability to accumulate in cells like hemin. This assay was clever, as the authors are able to draw parallels to the hemin and HCP1 relationship through visualization of the similar molecule ZP, with visualization of ZP being possible due to the autofluorescent property of ZP. ZP and HCP1 colocalized with each other, demonstrating that ZP is likely taken up by HCP1 in rat astrocytes. This finding is corroborated by another experiment by the authors demonstrating that hemin can rapidly accumulate in cells due to this transporter, as HCP1 has a high binding affinity for protoporphyrins compounds. Li et al. (2017) corroborates finding that ZP had the ability to be taken up into cells via HCP1 by observing a strong cellular fluorescence after about 2 hours of incubation. To bolster their findings, it was also demonstrated that when HCP1 expression was reduced there was a significant decrease in heme uptake. This reduced function phenotype is able to be rescued by complementation of HCP1 heterologous expression in murine hippocampal neurons. Hippocampal neurons were also found to have the ability to take up increased amounts of hemin in a time and concentration dependent manner (Li et al. 2017). In both experiments, the ZP was able to accumulate in cells through HCP1 while the iron and HCP1 concentrations fluctuated. Therefore, it can be concluded that uptake of hemin through HCP1 is can be visualized through the uptake of ZP.

Li et al. (2017) also examined whether psychological stress had any effect on HCP1 expression by regulation of corticosterone in rats. Corticosterone is a stress mediator hormone in rodents as cortisol is in humans (Joëls et al. 2018). They found that corticosterone treatment of rat cells resulted in the increase of HCP1 transcription, which was concurrently found with an increase in intracellular iron as well. To further corroborate the notion that hemin-bound HCP1 endocytosis is occurring at an increased rate when exposed to cortisol, it was also found that HO1 concentration was increased, indicating that hemin breakdown is occurring. Enhanced transcription and expression of HCP1 has the potential to increase hemin uptake into cells, leading to speculations of how the stress response is implicated in hemorrhagic stroke recovery.

**Hemin Cellular Uptake Mechanism Three: *Lipid Peroxidation***

Hemin is known to contribute to the oxidation of lipids in the cell membrane (Robinson et al. 2009). Accumulation of hemin is able to change the morphology of a cell. Kozlova et al. (2014) demonstrated this by adding varying amounts of hemin to erythrocyte (RBC) cultures. The membrane of an RBC is composed of a lipid bilayer and a cytoskeleton network. These two components are connected by a spectrin network where ankyrin and protein 4.1R keep the lipid bilayer and cytoskeleton linked (Kozlova et al. 2014), Filamentous spectrin networks have been found to contain 3% of the total proteins in the brain membrane, emphasizing its importance to the membranous structural support (Bennett et al. 1982). Deficiency of these proteins in the cell is known to contribute to membrane instability of the cell membrane. This was demonstrated in their experiment where hemin was able to alter the structure of the protein 4.1R and destabilize its links between the cytoskeleton. Hemin exposure also provoked the spectrin tetramers to disassociate into dimers, which resulted in the loss of their rope-like structural integrity (Kozlova et al. 2014). It was clear that hemin exposure resulted in the degradation of the spectrin network by evidence of membrane flickering, the structural fluctuation of a membrane, likely contributing to the destruction of the RBC cell membrane. Furthermore, peroxidative cross linking of the spectrin network occurred in a hemin concentration dependent manner. Cytoskeletons that were exposed to hemin lost their normal cell shape in a time dependent manner, further speculating that hemin can facilitate its own uptake by inducing membrane instability.

Hereditary spherocytosis (HS) is a genetic disease that alters the shape of RBCs and lessens their lifespan, however, this is distinct from other RBC shape-altering diseases such as Sickle Cell Anemia (SCA). The spectrin network in HS cells disassociates from the cell membrane through protein-protein interaction inhibition, such as the interaction between spectrin and ankyrin (Miraglia del Giudice et al. 2001). HS RBCs are also known to have a spherical morphology as compared to a disc shape and are known to have increased osmotic fragility (Zhang et al. 2013). This in turn contributes to the loss of homeostasis, which increases the likelihood of cellular death in the event of a stress response being intitiated by an exogenous stimulant. Accumulation of hemin has detrimental effects on the spectrin network of RBCs. Hemin oxidizes spectrin, and high amounts of hemin are present following a hemorrhagic stroke; resulting in hemin-dependent spectrin oxidation and disassociation, leading to the mechanical abberation of the membrane. Without the resistance that the cell membrane provides to stop compounds and other things going into the cell, hemin uptake is facilitated through a weakened cell membrane inititated by excessive hemin exposure.

There are several properties of hemin that contribute to the peroxidation of lipids including its high lipid solibility, hydrophobicity, and net positive charge (Robinson et al. 2009; Wagener et al. 2003). However, hemin may not just contribute to membrane instability through lipid peroxidation, but also through the oxidation of membranous proteins. It was demonstrated that hemin treated serum oxidizes the proteins within the low-density lipoprotein (Camejo et al. 1998). Perhaps synergistically, these properties of hemin allow it to weaken and bypass the membrane.

Discussion

The hemin-hemopexin complex, made of two substances that have a high affinity for each other, can be internalized through the process of endocytosis and multiple studies have found that the presence of hemin less to an increased presence of hemopexin and the LRP1 receptor, which will bind to the complex to internalize it. The HCP1 protein is speculated to be attracted to protoporphyrin rinds and not heme/hemin specifically. Its presence, however, is thought to internalize hemin due to the increase of heme oxygenase (protein that breaks down hemin) levels in the cell. It was also found in hippocampal neurons that as HCP1 concentration was reduced, there was a significant decrease in heme uptake. Another property of hemin is its ability to peroxidize lipids, which significantly affects the phospholipid cell membrane; when hemin comes into contact with the membrane, it will weaken its spectrin network and structural integrity, leading to osmotic fragility and eventual loss of homeostasis.
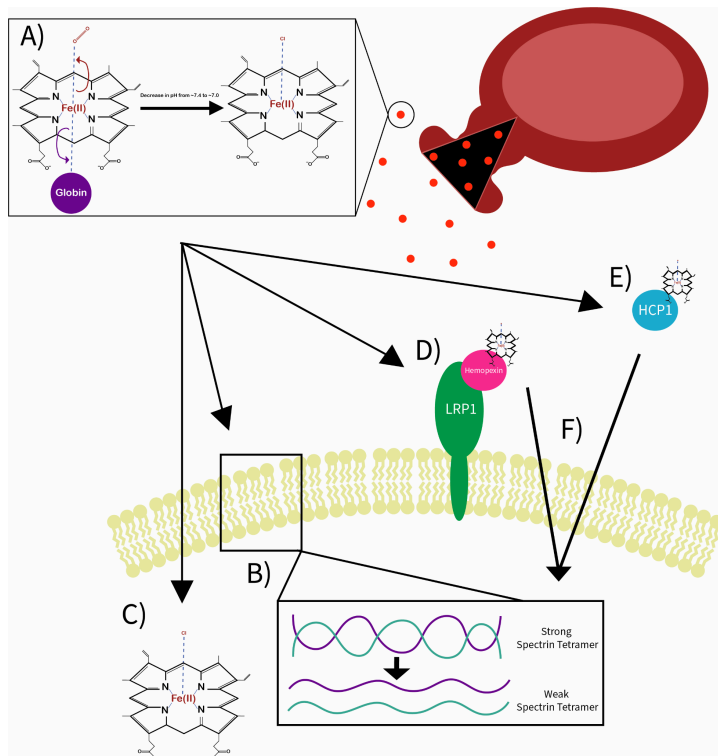
Figure 1. Putative Compensatory Mechanisms of Hemin Cellular Uptake. **A)** Heme oxidizes into hemin when it disassociates from global and loses covalence to free oxygen, going from an Fe2+ molecule to an Fe3+ molecule. **B)** The peroxidative property of hemin will immediately oxidize the spectrin filaments present in the cell membrane, weakening the structure of the membrane from strong spectrin tetramers to loosened ones. **C)** These loose spectrin tetramers render the membrane susceptible to osmotic fragility as the structure of the membrane will weaken. **D-E)** Hemin binds to hemopexin with an extremely high affinity, making a complex, which is then bonded to LRP1. Hemin also bonds to HCP1 to go into the cell. **F)** Once the

hemin-hemopexin complex bonds to LRP1. It will be internalized into the cell through the process of endocytosis.

As the cell membrane peroxidizes and weakens, we speculate that hemin will internalize at an extremely slow rate, with large amounts accumulated outside the cell going in slowly. All of the receptors and methods mentioned above work simultaneously in order to internalize as much hemin as possible. First, lipid peroxidation occurs, as the oxidative ability of hemin cannot be avoided. After, the HCP1 protein and the hemin-hemopexin complex will form and bind to LRP1 to internalize into the cell. We propose an experiment to test this speculation, where we use the technique of Western blotting to check hemin levels of a cell culture at different points in time. A cell culture will be exposed to hemin and then monitored at different time points to check hemin levels according to the different receptors. If hemin concentration through each follows the same curve after the initial exposure, all of the receptors work in conjunction with each other. If there are peaks of hemin internalization for each of the receptors, then that suggests that there is a primary mechanism of internalization through a high increase and a stronger expression [than the other mechanisms]. Any increases after that point would suggest secondary and tertiary mechanisms. It could also occur that lipid peroxidation happens slowly (passive diffusion), but hemin is internalized quickly, which could in itself suggest that the receptors work simultaneously. If all receptors internalize hemin at the same time, they are complimentary to each other; if they pick up at different times, they are compensatory. Different questions do arise from this study of what would happen in the case of a micro bleed. Another is if the same process and receptors would work in different parts of the body.

Acknowledgements

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A Literature Review on the Connection Between Background Music and Mathematical Performance By Katherine Pyasik

Abstract

Humans have long relied on music as a means of self expression. Frances Rauscher recently discovered a phenomenon termed "The Mozart Effect", and described it as an increase in spatial-temporal reasoning when listening to a Mozart sonata. Since then, a plethora of research has been conducted on the connections between academic achievement and musical instruction/background music (BM). There are also fundamental similarities between music and mathematics in disciplines, which some have proposed as an explanation for the observed positive correlation between musical and mathematical skills. Overall, the review yielded diverging results within age groups; as a result, no specific recommendations were able to be provided, but some recommendations are provided for the implementation of BM into educational settings.

Introduction and Background Information

Humans have long relied on music as a means of self-expression, dating back to early man's storytelling accompanied by drum playing. Music influences our thoughts, perceptions, and emotions and has the potential to better our memories. Humans also have biological roots in music, as infants have inborn capabilities that allow them to differentiate between pitches and remember melodies, so music instruction has the potential to improve cognitive capacity and communication skills (Yoon). Music instruction and background music (BM) have various profound effects on the brain's executive functions, overall cognition, and short-term processing ability (Jenkins; Kesan 3-4; Taylor & Rowe 51-52; Yoon; Barac et al.; James et al.).

The Mozart Effect

The Mozart Effect is a phenomenon discovered by psychologist Francis Rauscher in 1993; it showed that listening to Mozart's double piano sonata K448 for ten minutes produced short-term improvements in spatial-temporal reasoning. The subjects exhibited an 8-9 point increase in spatial IQ after listening to Mozart than after following relaxation instructions (Jenkins; Kesan 3-4; Taylor & Rowe 51-52). Spatial-temporal reasoning is defined as the ability to visualize and mentally manipulate objects in three dimensions, and developing this skill can be immensely beneficial in succeeding in fields of work that require complex scientific reasoning such as architecture, mathematics, and engineering (Taylor & Rowe 52). One neuroscientific explanation for this is that listening to music activates the prefrontal, temporal, and precuneus regions of the brain, which are the same areas that are activated when one engages in a spatial-temporal task (Jenkins).

Further attempts have been made to explain how Mozart's sonata impacts brain activity. One study, essentially replicating Rauscher's study, recorded brain activity via an EEG machine while participants performed a paper folding and cutting task, the same spatial-temporal task that was used to produce the findings of Rauscher's original study. It was found that the sonata

increased the firing power of neurons in the regions of the brain responsible for spatial-temporal tasks (such as the right temporal, left temporal, and right frontal regions) for 12 minutes after music exposure (Jenkins).

Extensive research into the effects of Mozart's sonata on the brain prompted the proliferation of literature on the exclusivity of this music's properties. Computer analysis was run on 81 selections of Mozart and selections of Mozart, J.C. Bach, J.S. Bach, Chopin, and 55 other composers. It was determined that Mozart's music, along with both Bachs', has a high degree of long-term periodicity and contains emphasis on the average power of particular notes. Contrastingly, the minimalist music of Philip Glass and old-time pop music did not show long-term periodicity and, therefore, would not produce a Mozart effect (Jenkins). Another study that looked at epileptiform activity found that exposure to Mozart's music could lower continuous bilateral spike and wave complexes (which are characteristics of epilepsy) by 50% (Jenkins; Chabris et al.).

A number of studies that potentially disprove the Mozart effect have come to light in the years following Raucher's 1993 study. These posit that intelligence is increased when a student learns to play a musical instrument, as this requires stimulation of 80 to 90 percent of the brain's motor control capabilities and, therefore, that children who learn to play musical instruments tend to develop highly refined control of the brain, which strengthens the entire brain's capabilities (Yoon). These studies state that music does not increase overall intelligence when referring to the consumption of music, opposed to musical instruction. Multiple experiments across universities, including Chabris' study, were conducted in an attempt to replicate Raucher's original Mozart effect experiment, and participants' IQ scores were measured before and after exposure to Mozart's sonata K448. It was found that there was no significant difference between the times scores were measured, and the authors suggested that Rauscher's original theory may be false (Chabris et al.).

Rauscher's 1999 article in the journal *Nature* responds that Chabris' method of analysis led to the assessment of changes in abstract reasoning tasks other than spatial-temporal tasks, which likely unfavorably skewed his results since Raushcer's sole claim was that Mozart's music benefits spatial-temporal reasoning. Additionally, Chabris argued that the Mozart effect is a product of "enjoyment arousal", an idea that attributes the Mozart sonata's benefits to its listeners' deriving pleasure from listening to it. Several experiments, however, suggest that this is untrue. In another study by Rauscher, students listened to works of Mozart and Mendelssohn, reported that they derived greater pleasures from Meldelssohn's work, and still demonstrated a Mozart effect (Chabris et al.). The previously mentioned study on epilepsy also demonstrates this, as the decrease in bilateral spike and wave complexes was present in a comatose patient, showing that the Mozart effect is not a product of "enjoyment arousal" (Jenkins). Similarly, when rats were in the presence of Mozart's music both in utero and after birth, they were able to find their way through a spatial-temporal maze with fewer mistakes than the control group and it is not plausible that this was due to their enjoyment of the music (Jenkins; Chabris et al.).

Music Instruction and Mathematical Performance

Researchers at York University aimed to establish the connection between music education and untrained tasks (such as verbal and spatial intelligence, which are significant predictors of achievement in school and productivity at work). The researchers created two curricula, one on music and one on visual art, and administered each one to separate groups of students aged 4-6. An increase in verbal intelligence was determined only among the music education group. It is posited that this is because music training activates brain regions that are important to language processing, including those at the subcortical (auditory processing) and cortical (implicit processing) levels (Barac et al.). Additionally, it was confirmed that piano instruction yields benefits in older adults such as strengthening verbal memory and increasing functional and structural brain plasticity, characteristics that slow brain deterioration into diseases like Dementia. Atrophy of the hippocampus (a part of the brain vital to relational memory) is common among those eventually diagnosed with dementia, and partaking in music instruction can help preserve it (James et al.).

Despite a plethora of literature suggesting that music instruction always yields benefits, certain study designs undermine these conclusions. For example, studies that compare musical groups and non-musical groups are generally less effective than those that introduce music instruction to one group in the study for the first time. This is because certain personality traits may predispose individuals to be more likely to begin and follow music lessons. Therefore, these individuals may have naturally better spatial-temporal reasoning skills and a higher intelligence quotient, so if they are tracked for a period and compared with a non-musical group, their naturally higher IQ may prevail and would not be able to be attributed to their musical experience (Barac et al.). It is important to note this as a possible limitation of studies used by previous researchers that have come to the conclusion that musical instruction improves mathematical performance.

Connections Between Mathematics and Music

There is literature supporting the idea that mathematics and music are interconnected domains and require similar processing patterns in the brain. One literature review by professors at Cornell University and Williams College posited that introductory statistics courses became more difficult to teach when statistics changed from being a mathematics course to being its own discipline. Statistics is not a self-contained and self-consistent field like mathematics because not everything that students need is laid out before them. With this in mind, the authors compare mathematics to music because prodigies (from Gauss to Mozart) develop in these fields; prodigies do not, however, develop in subjects such as statistics and literature because these domains are not isolated and self-consistent, and therefore are harder to comprehensively grasp (Velleman).

Aims and Purpose

Many educators report that they believe that some of their students perform poorly due to a lack of interest in the subject they are studying. Additionally, academic performance may be inhibited by stress during examinations. One researcher suggests that the Mozart effect works during academic tests because the music helps students overcome stress due to cognitive

dissonance, although this is contradicted by *Rauscher 1999*. Therefore, overcoming this type of stress is vital for the accumulation of knowledge and scientific advancement (Cabanac et al.). The nonfiction book *Essentialism* by Greg McKeown discusses this issue from the lens of productivity. McKeown states that, when students are labeled as "bad at math", they see only two options: to neglect trying or to put all of their energy and effort towards becoming better. This is termed "learned helplessness", as there is a perceived lack of options. McKeown says that this can be combated if students figure out how they learn best and, from there, optimize their learning techniques (McKeown 37).

Considering the profound power of music to influence human thoughts, the emergence of issues in learning patterns, and the general importance of mathematics scientific development, it is important to look at the intersection between these topics. Therefore, this literature review's aim is to provide a recommendation on the integration of background music into mathematics education.

Results

Elementary and Middle School Students

It is important to note that nearly all of the research accessed on this age group discussed music-based lesson plans, rather than simply listening to music while the students worked. It is being included regardless as the students who took part in these studies did listen to music while they learned mathematics and while doing practice questions. These papers were judged to be different from those that looked at the correlation between musical and mathematical proficiency because they do not discuss musical instruction.

One study detailed the results of the introduction of music into the lesson plans of third-grade students diagnosed with Moderate Learning Difficulties (MLD). Using pre-tests and post-tests, the researchers evaluated whether the introduction of Individualized Education Programs (IEPs) supported by musical activities improved the participants' subtraction and addition skills. The researchers noted that, in general, subtraction was more difficult for the students than addition, but there were significant increases between pre and post tests after the music-supported IEPs were implemented (Korkaz & Temur 433). A literature review study identified that one New York City program called LEAP (learning through an expanded arts program) has been successful in using music-inspired lessons to reinforce elementary mathematical concepts. It is noted that this program also boosts students' self confidence in their mathematical abilities, which alleviates math anxiety (Yoon). A similar study to *Korkaz & Temur* used the programs MusiMath and Academic music to train students on fractional concepts. No statistical differences in fraction computational ability were found between the two intervention groups, and both intervention groups out-performed the control group on 3 and 6 month check-ins post-intervention. Additionally, MusiMath (a holistic music program, opposed to Academic Music, which only used rhythm to reinforce mathematical concepts) spurred greater understanding of untrained fractions, such as one-third and one-fifth. These were untrained as

only one-half, one-fourth, and one-eighth were taught to the students since it is easier to draw an analogy between these fractions and musical notes and rhythms (Azaryahu et al.).

In another study, researchers found that listening to background music (BM) increased response speed but not accuracy in children aged 10-12 when solving math problems. The researchers used the arousal hypothesis to explain their findings, stating that the BM was perceived as relaxing and had a positive effect on the number of math problems completed and the pro-social behavior of the participating students (De Benedetto et al.). Another paper mentions the Yerkes-Dodson principle, which states that if a task is complex or unlearned, deterioration of concentration occurs more quickly. Some research has shown that positive emotions (which could arise with BM) can adversely affect cognitive reasoning tasks, including math problems. Finally, one paper examined the impact of relaxing music and aggressive/invigorating music on mathematical performance in students ages 10-12. It looked at relaxing music and, although the difference between the music and non-music groups wasn't statistically significant, the average math test score with music was 84 and without music was 80. Additionally, there was considerable individual variation within the music group. Just like the study described in this paper's introduction, having calming music in the background increased the speed at which students solved arithmetic problems, but did not significantly increase the instance of correct responses. (Hallam et al.). A study from Bowling Green State University was conducted to gauge students' feelings, thoughts, and physical responses to listening to Mozart while taking a mathematics exam using pre-test and post-test surveys in an attempt to address test anxiety. Out of the six students with test anxiety, four reported that they obtained positive emotions from the music during the exam and had a positive effect on performance. Out of all the students, 68% reportedly believed that the music had a positive effect on their scores and 64% said they prefer to listen to Mozart while taking exams, and only 4% (1 student) reported that they would rather take the exam in silence. The author recommends that schools allow students who prefer not to listen to music to take their exam in a back room where it is silent (Blevins).

<u>Secondary School and College Students</u>

One study was conducted on regular and accelerated Algebra 2 classes where students listened to classical music, rap, rock, or no music. The researcher posited that the students enjoyed listening to music during their test since many of them reported listening to music while doing homework; to emulate this setting as best as possible, the researcher chose to play popular songs that the students likely knew. All music improved performance, but listening to classical music provided the more significant improvement, followed by rock and rap respectively. The author speculated that this occurred because classical music had no distracting lyrics and blocked out normal distractions, while rap music's lyrics were just as distracting as the background noise in the normal test-taking environment (Maas). Psychologist Daniel Kahneman's cognitive capacity model, however, argues that people's attentional resources are depleted when they are doing multiple things at once, so classical music would likely provide a similar distraction to rap music as well (De Benedetto et al.). Another study published in Vanderbilt University's Young

Scientist Journal involved both a randomized control trial (RCT) in which the participants were randomly assigned a testing condition (with or without BM) and a preference control trial (PCT) in which the students choose their testing condition. This study was conducted online during the period when most high schools were virtual, so the students had complete control over the music that they listened to. The testing condition did not influence test scores. However, although the two testing conditions did not have significantly different finishing times, those who reported listening to music while studying or testing usually finished faster. Additionally, the students who chose to test in silence finished significantly slower than those randomly assigned to silence (Adams).

There is also literature on the effects of BM on college students' mathematics performance and it yields divergent results. A study from the International Journal of Primary Education aimed to find out how listening to classical music, softrock, pop music, and nature music affect college students' performance on exams testing limits and derivatives. When tested on limits, the researchers identified that softrock, pop, and classical music can help answer questions correctly. Nature music was only played during the derivatives test, and it was found that it does not help if it was a student's first preference, but it does help if it is at the end of a student's preference list. In the derivatives topic in general, solving problems with music helped to answer questions correctly (Kesan 3-4). Another study that showed a positive correlation between BM and mathematical performance was done on three college trigonometry courses. Although the original Sonata that showed the Mozart effect in Rauscher's study was not used, this study still upheld the Mozart effect: students performed significantly better when Mozart was being played as background music during their exam. The college students' SAT scores were also collected to ensure that there was no difference between the baseline intelligences of the control and experimental groups, which adds to the validity of this study (Taylor & Rowe 58). Another study aimed to find out whether agitating, happy, or touching music (opposed to environmental sounds or silence) was beneficial in helping college students solve difficult arithmetic problems. This study found that silence was detrimental in solving difficult math problems, and that the participants who were introverts were faster at solving problems in silence, but when rain sounds were added extroverts were just as fast. Additionally, reaction times for extroverts were faster during agitating or joyful music and rain sounds, while for introverts reaction times were faster during agitating music (De Benedetto et al.). Finally, a Filipino study sought out the correlation between listening to pop music and academic (including mathematical) performance. The time that the students spent per week listening to music per week (and the amount of time spent listening to pop music per week) was shown to have a positive effect on mathematical performance (Tiu).

A 1999 study on college students who were non-music majors was done to see if classical or pop music affects their math performance. The results showed that there was no statistically significant difference between the control and experimental groups and, therefore, that math test scores with no background music were significant predictors of math test scores with classical and pop music playing in the background (Mantei & Kelly 40).

Synthesis of Results, Conclusions, Recommendations

The literature accessed on elementary and middle school students shows conflicting results. Programs that used music to teach mathematics (like LEAP, Academic Music, and MusiMath) measurably improved music performance (Yoon; Korkaz & Temur 433; Azaryahu et al.), but two other studies showed that there were no statistically significant differences between BM and non-BM groups in middle schools (De Benedetto et al.; Hallam et al.). In a study of 24 students, the majority said that they enjoyed listening to Mozart while taking tests because they believe it improves their performance (Blevins). The participants in this study listened to Mozart's music, and, although no quantitative data for music and non-music groups was given, it is reasonable to conclude that a Mozart effect may have been present since the students reported enjoying it and believing it boosted their performance. Based on this, it is reasonable to conclude that BM music likely does not affect middle school students' mathematical performance, but there is still not a wide enough variety of evidence to support this assertion, as only two sources were accessed for this age group. From this literature review alone, it is reasonable to draw the conclusion that BM helps improve mathematical performance in elementary school students, but it is not certain whether this improvement is derived from using music to teach mathematics or listening to BM while completing math problems. This uncertainty mainly stems from the fact that no sources that had music and non-music groups taking the same mathematics assessment for the elementary age group. The same is true for middle school groups, as no studies that showed statistically significant differences between music and non-music groups were uncovered. The results for this age group as a whole lend themselves well to the position that Mozart's music may improve spatial-temporal reasoning skills, and that other music does not have the same properties (Jenkins). This connection may be related to the fundamental interdisciplinary connections between mathematics and music that *DeVeaux & Velleman* discussed.

The results in high school students proved to be divergent as well: one study found that listening to classical music instigated a more significant benefit on mathematical performance, while another said that there was no difference between testing conditions, even when students got to choose the music they listened to and, as a result, likely derived more pleasure from it than if the researcher had chosen for them (Maas; Adams). A study that looked at university students identified that classical, softrock, and pop music can help students answer calculus problems correctly (Kesan 3-4), and another showed that Mozart's music can help college students with similar baseline intelligence answer math problems correctly (Taylor & Rowe 58). *Taylor & Rowe* upheld the Mozart effect. *De Benedetto et al.* found that extroverted and introverted students work through math problems quicker under difference musical conditions, but did not assess answer accuracy, *Tiu* identified that time spent listening to music is positively correlated with better mathematical performance, but not did not specifically address BM during testing, and a separate study on university students showed that classical and pop music do not affect math scores. For high school and university students taken together, a preponderance of the literature accessed points to the idea that BM does not significantly affect mathematical

performance, unless it is Mozart's music. This upholds previous literature (and Raucher's original hypothesis) that states that Mozart's music has special characteristics (i.e. long-term periodicity and emphasis on certain powerful notes) that give it its special properties that other composers' pieces do not have (Jenkins).

Based on the literature accessed for this review, no specific recommendations can be made due to the diverging results from all the studies accessed. Taken all together, however, the studies reviewed suggest that the Mozart effect is present across age groups, while other types of music can help students solve math problems quicker, but not necessarily more accurately. This upholds the Mozart effects that *Taylor & Rowe* and *Jenkins* identified. Therefore, the recommendation is that schools should implement an opt-in system of listening to Mozart while students complete math problems. If students feel that it would help their focus, they can opt in to listening to Mozart while they work. This recommendation stands for middle school through college age students, as studies showed that a Mozart effect is present in these groups (Blevins; Taylor & Rowe 58). This recommendation does not involve other music genres or classical music composers because the results were inconclusive for them (De Benedetto et al.; Hallam et al.; Maas; Adams; Jenkins). However, bearing in mind that this is likely infeasible and may create unjustified friction in testing environments, the secondary recommendation is to conduct more studies to see how BM affects mathematics performance. This would allow more specific recommendations to be made that are supported by a greater array of experimental evidence than those made by this study.

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Digital Harmonies: Analyzing Media's Interplay with Sense of Agency in Music Therapy
By Chloe Cho

Abstract

Music therapy is commonly used to improve the people's mental and physical health. However, the role social media plays in this therapeutic practice has not yet been thoroughly explored. The work of McFerran, who investigated the benefits of music therapy in a group of 40 young Australians, was used in this study (McFerran, 2013). Additionally, our research is informed by Saarikallio's work, which looked into how music affects the perception of agency in 44 adolescents (Saarikallio, 2020). Though these papers reveal the positive effects of music, they do not consider an important factor in their research– how much their subjects are exposed to media.

Introduction

Music therapy (MT) is a developing field in healthcare in which music therapists employ music in collaborative therapeutic settings with the aim of improving emotional, physical, and mental health ((O'Neill, S. A. (2017, June 26). *Music and social cognition in adolescence*. Routledge Handbooks Online.)). This method has become well-known because of its influence on the sense of agency, which is the perception of control over one's actions ((Saarikallio, S. H., Randall, W. M., & Baltazar, M. (2020, January 8). *Music listening for supporting adolescents' sense of agency in daily life*. Frontiers in psychology.)). Though music therapy is growing in its use as a method of treatment, there is still a lot to learn about the role social factors can play in a sense of agency in musical therapeutic practices.

We base our framework around researcher McFerran's observations on music's psychological and emotional benefits. 40 young Australians were asked to recall instances in which music did not benefit them compared to the instances when it did ((McFerran, K. S., & Saarikallio, S. (2013, November 27). *Depending on music to feel better: Being conscious of responsibility when appropriating the power of music*. The Arts in Psychotherapy.)). McFerran's study implies that adolescents turn to music for feelings of comfort.

The second study that this paper is expanding upon is the research by Saarikallio, Randall and Baltazar. In the study, the impact of music on adolescents' daily sense of agency as well as its contextual factors are examined. 44 adolescents were asked to self-report their music experiences during their everyday lives. The study recorded perceived levels of agencies and considered the situations, activities, and reasons for listening to music.

However, the possible omission of media and technology that interact with a person's therapy experience is a prevalent problem in this field of study. The impact of media and technology on the efficacy of music therapy cannot be understated in the digital age we live in. The selection of music streaming services, the importance of custom playlists, the influence of music in virtual spaces, and the incorporation of digital music creation tools are all elements that influence how one perceives the musical therapeutic benefits on the sense of agency. Future

studies should consider technology's role on adolescent mindsets so that the advantages of music therapy can be maximized in today's digital world.

The Effect of Music and Social Media on Adolescents

Social media platforms have changed how teenagers express themselves. 81% of teens state that using these platforms makes them feel connected to their friends' lives ((Atske, S. (2018, November 28). *Teens and their experiences on social media*. Pew Research Center: Internet, Science & Tech.)). More than that, they could express themselves by uploading pictures, videos, artworks, and music to present their interests. One in ten tweens (a child who is between the stages of childhood and adolescence) and adolescents (11% of tweens and 13% of teens) will use digital platforms to create art or music ((Rideout, V., Peebles, A., Mann, S., & Robb, M. B. (n.d.). *The Common Sense Census: Media use by tweens and teens, 2021*. Common Sense Media.)). However, social media can bring dangerous experiences as well. While individuals who express themselves on social media platforms display a strong sense of self-assurance, they may also encounter pressure to conform to societal norms. Additionally, though teenagers can engage in communication through online platforms, they can also be exposed to online harassment. As such, one characteristic of social media is its immense emotional influence, especially on teens. Although there is a significant number of adolescents who find support in these online communities, there is also a subset that encounters adverse experiences stemming from unpleasant interactions and comparisons to their peers.

A strategy to better teenagers' health is to employ music to set limits on social media use. Implementing music therapy can serve to urge teenagers to disengage from social media platforms at designated intervals. Adolescents who have an increased amount of time on social media are prone to psychological distress and depression ((Bozzola, E., Spina, G., Agostiniani, R., Barni, S., Russo, R., Scarpato, E., Di Mauro, A., Di Stefano, A. V., Caruso, C., Corsello, G., & Staiano, A. (2022, August 12). *The use of social media in children and adolescents: Scoping review on the potential risks*. International journal of environmental research and public health.)). However, the incorporation of music into their screen time activities may enhance their time management skills by serving as an outlet for their emotions. This hinders the tendency to disclose personal information over the Internet. Moreover, listening to music can create positive emotional states among adolescents. This evokes feelings of fulfillment among teenagers, which enhances their feelings of control. This idea is especially beneficial because it can mitigate some risks of social media.

Sense of Agency

The sense of agency is a part of human consciousness that focuses on how one perceives their control. It is integrated in everyday life, referring to how much power one has over their daily actions. People tend to feel a stronger sense of agency when being able to confidently perform an activity under their control ((Moore, J. W. (2016, August 29). What is the sense of agency and why does it matter?. Frontiers in psychology.)).

Sense of agency is a prevalent problem in people with health issues. For instance, agency is most researched in schizophrenia. In Daprati's study, healthy individuals and patients with schizophrenia were examined. They were tested on whether they would be able to decipher if their hand movements were theirs or the experimenter's, and the patients had more difficulty ((Daprati, E., Franck, N., Georgieff, N., Proust, J., Pacherie, E., Dalery, J., & Jeannerod, M. (n.d.). *Looking for the agent: An investigation into consciousness of action and self-consciousness in schizophrenic patients*. Cognition.)).

Positive and Negative Aspects of Social Media

Social media is a platform where adolescents can feel empowered. Sharing music on social media is a way for young people to express online spaces and indicate social affiliations ((Falconer, E., Snowdon, R., & Taylor, Y. (n.d.). *Queer youth, Facebook and faith: Facebook methodologies and online identities.* American Psychological Association.)). This use of music allows adolescents to create a social identity on social media. Since music has the special power of stirring up emotions in listeners, sharing music-content in social media can serve as a way to set up emotional connections between users and their followers. Sharing musical tastes also reflects the person's personality, giving them the opportunity to express themselves. Social media platforms make it possible for communities to bond and find their identities using music.Social media can enhance a sense of agency by serving as a platform for teenagers to connect and express themselves with others on social media.

According to Anne Marie Albano, particularly those with mental health issues have an inclination to spend an increased amount of time engaging in social media activities while decreasing their time physically interacting with others ((Matters, H. (2022, March 14). *Is social media threatening teens' mental health and well-being?* NewYork-Presbyterian.)). However, increasing time spent on social media can cause adolescents to develop neurotic tendencies. Neuroticism is characterized by an increased predisposition to experience harmful emotions, including self-consciousness, irritability, emotional instability, and depression ((Widiger, T. A., & Oltmanns, J. R. (2017, June). *Neuroticism is a fundamental domain of personality with enormous public health implications*. World psychiatry : official journal of the World Psychiatric Association (WPA).)). These emotions can cause an adolescent to perceive their personal agency differently. For instance, adolescents with high levels of neuroticism constantly worry about how they are viewed and whether they conform to societal norms, and comparing themselves to others online makes these neurotic tendencies worse. This can affect their agency by making them feel wary before making decisions because of their fears of being judged. Their desires to fit in these modern standards on social media may cause them more harm than good.

The Role of Influencers

Society's influencers have begun to impact how adolescents perceive themselves. According to SagePub Journals, there are around 44 million influencers worldwide all across social media ((Chopra, A., Avhad, V., & Jaju, S. (n.d.). Influencer Marketing: An

exploratory study to identify ... - sage journals.)). With the growing number of influencers, the effects on adolescents are only increasing. Though influencers work to promote lifestyles, their good intentions can inflict negative effects on their audiences. For instance, their influence can create unhealthy comparisons and expectations. These unhealthy comparisons may cause an individual's sense of agency to be affected, as they feel their sense of worth decreasing.

Lady Gaga and Taylor Swift create strong connections with their listeners through their lyrics and this leads fans to believe that they can relate to the artist personally. Even if the listeners have never met the artist physically, the connection that the songs convey serves to have a positive impact on listeners' social development.

In the study of researchers, Click, Lee and Holladay, Lady Gaga's fans, "Little Monsters," report that they feel close to Lady Gaga, their "Mother Monster," on a personal level due to her interactions with her fans on social media platforms. In her direct interactions, Lady Gaga validated her fans, helping these fans feel a stronger sense of self-identity and an increased feeling of self-worth ((Click, M. A., Holladay, H. W., & Lee, H. (n.d.). Making monsters: Lady Gaga, fan identification, and social media.)). These interactions further demonstrate the impact influencers can have on the development of fans' identities.

Coping and Socio-Emotional Communication

Music can serve as an adaptive or maladaptive coping mechanism that affects adolescent's neuroticism. Though music can have positive effects when helping manage emotions, it can sometimes have negative effects and cause an unhealthy dependence on music. Adolescents who develop this unhealthy habit may show a decrease in their sense of agency as they begin to focus their lives solely on music.

Understanding more about the sense of agency is an important field of research to further discover the science behind behavioral changes. Turel discovers that people experienced a stronger perceived agency when restraining themselves from social media use ((Turel, O. (2020, October 1). *Agency over social media use can be enhanced through brief abstinence, but only in users with high cognitive reflection tendencies*. Computers in Human Behavior.)). Being on social media too often causes adolescents to lose their self-confidence. However, relighting this sense of agency is important for therapists to help their patients set limits for their time on social media. Turel suggests that a way to restore a sense of agency is by experiencing abstinence. However, he does not consider the possible application of musical therapy to strengthen feelings of agency. Although abstinence is a treatment to this problem, music therapy can give more benefits than simply limiting social media time. For instance, music therapy can give adolescents the opportunity to discover their creative identities and find their passions.

Personal Taste in Music

Understanding the connection between musical taste and behavior can expand research on how behavior functions ((Rideout, V., Peebles, A., Mann, S., & Robb, M. B. (n.d.). *The Common Sense Census: Media use by tweens and teens, 2021*. Common Sense Media.)). For

example, some songs have lyrics centered around risky behaviors like drug use, violence, misogyny. Exposure to these lyrics can cause a negative impact on adolescent mindsets. "Young people who viewed risk behavior presentations in social media overestimated the extent to which their peers engaged in these risky behaviors (Black et al., 2013), thus likely developing skewed risk behavior norms and increasing their likelihood of engaging in them" ((Elvers, P. (2016, January 20). Songs for the ego: Theorizing musical self-enhancement. Frontiers in psychology.)). As highlighted by Black, adolescents who are often exposed to risky behaviors in the media may develop warped perceptions of society's norms. This altered perception may influence adolescents to involve themselves in dangerous activities.

However, sometimes, musical lyrics can be empowering. Songs with energetic, strong, and cheerful lyrics may inspire adolescents and instill positive emotions in them. These songs can also provide adolescents with positive insights on life ((Bobkowski, P. S., & Pluretti, R. (n.d.). Social media, adolescent developmental tasks, and music . Academic.oup.com.)). Artists like Rihanna, Lady Gaga, and Pink aim to express the positive aspects of themselves through the lyrics in their music.

The Therapeutic Benefits of Creating Music

People create music all the time, but not many of them know about the impact this could have. Ways people can create music include beat-making, starting to learn how to play an instrument, creating a monologue in music, composing, and more. Beat-making (creating metrical rhythms on a digital audio workstation) allows adolescents to express their emotions in the beats they write. They can showcase their feelings through rhythms and melodies, allowing them to express themselves when they cannot in words. Having the freedom to experiment with these beats can aid adolescents in feeling a sense of control, as the notes being written are under the adolescents' control. Moreover, the music styles they create may allow adolescents to discover what kind of person they wish to be. This can especially be beneficial after their sense of worth is decreased from constant exposure to unrealistic standards in social media. With their own beat-making music, adolescents can discover their identities beyond what they fake on social media. Creating music can healthily set a boundary between teenagers and social media.

Technological Influences on Music Therapy's Efficacy in the Digital Age

Since technology was created, it served to be an efficient and accessible way to perform music therapy. For instance, through online platforms such as Spotify, Apple Music, and more, people can access music therapy without having to go to a certified clinical doctor. Moreover, a contributing factor to music therapy's success is the fact that music can be selected and modified. To give an example, on Spotify, people can add whatever songs they would like that would address their therapeutic goals.

Technology can also be used to connect people with various musical therapy experiences. Social media groups may serve to be beneficial towards music therapy users as they feel supported and comforted. For example, on Instagram, there could be Instagram group chats made

with the intentions of connecting people with similar beliefs and hobbies. This can instill feelings of acceptance and make the people in the communities feel less lonely.

Future Directions

The author of the present study conducted studies through her nonprofit organization to research the effectiveness of music therapy. She performed songs like "Can't Help Falling in Love" and "My Way" for patients in local hospitals. Observing the patients' reactions showed her that music can not only serve as an alternative treatment to health issues but also promote a healthy mindset amongst adolescents. Due to some features of social media, many adolescents are prone to feeling negative views of self-worth. However, adolescents can use music to combat these issues.

For instance, adolescents can create playlists with songs they can resonate with. However, it is important to consider the lyrics of the songs and what kind of message they are trying to convey.To give an example, some songs with churlish lyrics can negatively influence adolescents. On the other hand, listening to songs with positive lyrics can give them a sense of encouragement and positivity. A way to spread positive musical genres is by sharing playlists. Because of social media, teenagers can feel a decrease in their sense of agency, as they are prone to self-comparisons with unrealistic standards. However, a way to combat these standards is by utilizing music. With music, they can limit their time spent online.

"Musicking" can be correlated with the notion of a sense of agency and music therapy within the framework of this research. "Musicking" refers to when individuals participate in the creation of music, emphasizing that music can be much more than just listening. Patients can feel a stronger sense of the control they have in their lives through musicking.

Researchers can empower adolescents to begin to take control and manage their own lives, their emotions, and their boundaries with the social media world with further research.

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The Influence of Stress and Anxiety on DNA Methylation: A Review By Ariana Fatima Naqvi

Abstract

Epigenetics (DNA modification), specifically DNA methylation, has become a more popular field to be studied in recent years. DNA methylation is a common mechanism of epigenetics where a chemical methyl group blocks certain parts of the DNA, which can result in no gene expression. Its relation to stress and anxiety is important to discuss since many individuals struggle with their mental health. Stress and anxiety can promote DNA methylation in an organism, which in turn can cause gene expression that is typically negative. Therefore, the link between these negative expressions such as physical illnesses, can be identified by studying epigenetics. This review dives deeper into DNA methylation as well as stress and anxiety through the analysis of nine different studies. This includes longitudinal studies, analysis of BDNF methylation, OXTR methylation, GR methylation, hypothalamic DNA methylation, different early-life stress experiences, and the reduction of methylation. The primary limitations and future directions of this field are also discussed.

Introduction

Epigenetics is broadly defined as modifications to the DNA without altering the DNA sequence itself (Conradt, 2017). These modifications result in gene expression due to the alterations to the chemical nature and composition of genes (Meaney, 2010). The three main, essential epigenetic mechanisms include histone modification, RNA regulation, and DNA methylation (Conradt, 2017). Histones are the proteins that DNA wraps itself around, and when histones are packed together tightly, it makes the DNA less accessible. Thus, the protein "reading" the DNA cannot access it, essentially turning the gene "off". Vice versa, histones can be packed loosely, allowing genes to be turned "on". Therefore, the modification of histones can determine how tightly or loosely the histones are packed, which controls whether the gene is expressed or not (Conradt, 2017). The second mechanism, RNA regulation, refers to the use of RNA in gene silencing by allowing or destroying the development of proteins from coding RNA. This again controls gene expression (Tchurikov, 2005). Finally, the last mechanism is DNA methylation, which can be considered the most studied epigenetic mechanism in terms of behavioral studies (Conradt, 2017). In DNA methylation, a chemical or "methyl" group is added to certain sites of DNA, blocking the proteins from "reading" it. The opposite can occur as well, where a methyl group is removed, allowing the gene to be turned "on". This review will be mainly focusing on DNA methylation specifically instead of the broad field of epigenetics, due to its commonality in credible studies. DNA methylation is most common due to its essential role in organism development compared to the other mechanisms. It is responsible for X-chromosome inactivation as well as creating specialized body cells (Jin et al., 2011).

In recent years in this field, a relationship between epigenetics and mental health has been discovered by researchers. Chronic stress can induce genetic expression in the adult brain

through epigenetic modifications (Nestler, 2016). This field is important to study because stress and anxiety are common mental health issues that individuals face, and by learning more about their relationship with DNA methylation, stress can be prevented from negatively influencing the human body. Also, when more is discovered about epigenetics, it contributes to altering long-lasting theories and perspectives that are fundamental to biology. As more is discovered about epigenetics, more scientists are starting to question the Central Dogma of Biology (Saade & Ogryzko, 2014). The Central Dogma explains the flow of genomic information in cells, simply saying DNA creates RNA, which in turn makes proteins. Epigenetics is now questioning the rigidity of this process (Wang & Allard, 2022). By continuing to learn more about the field of epigenetics, experts can find important discoveries that contribute to the basic understanding of biology as a whole. One way of learning more about epigenetics is by analyzing its relationship with other factors, such as mental health. Overall, many studies that have been done analyze how stress and anxiety promote epigenetics, more specifically DNA methylation. But in order to take a look at these studies, it is important to establish a basic understanding of what DNA methylation specifically is.

What is DNA Methylation?

DNA methylation typically occurs at the 5' end of a gene, which is called the promoter (Mitchell et al., 2016). A variety of areas of a gene, including the promoter, consist of dinucleotides that include a cytosine-phosphate-guanine site, abbreviated as CpG. Areas of heavy CpG are named CpG islands. At this site, the "C" is most likely to be modified through methylation. A methyl (CH_3) group is added to the 5' end of a cytosine, which forms 5-methylcytosine (Mitchell et al., 2016).

The process of DNA methylation prevents the transcription of the DNA, which leads to the silencing of gene expression (Overbeek et al., 2020). The methyl group psychically hinders transcriptional proteins from accessing promoter regions, suppressing gene expression (Hossack et al., 2020). DNA methylation is also a stable modification, though sensitive in terms of environment, meaning that any environmental influences can cause biological effects (Womersley et al., 2022). In terms of mental health, specific genes have been gaining more attention in the epigenetic field that relates to stressful experiences promoting anxiety symptoms. For instance, genes such as FKBP5 and GR (glucocorticoid receptor) are negatively related to feedback of the HPA axis. The HPA (hypothalamus-pituitary-adrenal) axis is the central stress response system, and these genes interfere with this response system, causing the likelihood of developing anxiety symptoms as a result of stressors (Hua et al., 2023).

What is Stress and Anxiety?

Though stress and anxiety are commonly used interchangeably amongst people, they are two very different processes. A stress response derives from a threat (stressor) in which an organism responds in a frantic or alarmed state (Daviu et al., 2019). Common day stressors include losing a job, facing a lot of pressure, going through a divorce, or being overloaded with

work. The organism's reaction involves a combination of both physiology and behavior, which can also lead to physical bodily changes. However, perceived threats involve the concept of anticipation, which is what sets anxiety apart from stress. According to *The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5), "...anxiety is the anticipation of a future threat" (Daviu et al., 2019). The impact of stress can influence the development of anxiety symptoms in a human, especially early life stress. Any late-life anxiety symptoms can derive from early life stress, such as maltreatment exposure, poverty, divorced parents, a family member's death, and more. A study conducted by Lähdepuroet et al. (2019) found that physical and emotional traumas from childhood, as well as low childhood socioeconomic status, were associated with higher anxiety symptoms in adulthood. The reason why early life stress is so impactful on later adulthood is because a person's childhood is when the most biological changes occur, such as the remodeling of the brain or neural plasticity (Smith & Pollak, 2020). Early-life stress (ELS) also has a major impact on other factors of human beings, not just anxiety. Early-life stress is also associated with other mental health disorders such as severe depression, PTSD, and bipolar disorder (Syed & Nemeroff, 2017). Early-life stress can also lead to physical health issues, such as a higher risk of early death or illnesses such as cardiovascular disease (Taylor, 2010). The influence of early life stress on a person is partially due to DNA methylation, which allows for changes in the brain or the development of physical/mental disorders.

**Stress and Anxieties Influence on DNA Methylation**

Stressful experiences in childhood have the potential to cause modifications to one's epigenome (Fachim et al., 2021). A variety of studies have been done to assess how early-life stress and anxiety can influence DNA methylation. Many experts conduct these studies in different ways, such as using rodents versus humans, using longitudinal studies, or studying brain methylation. Another method for these studies is analyzing specific genes, which is what Unternaehrer et al. (2012) did. These authors conducted a study that analyzed DNA methylation levels before and after a psychosocial stressor in two different stress-related genes: oxytocin receptor (OXTR) and brain-derived neurotrophic factor (BDNF) (Unternaehrer et al., 2012). This study consisted of 76 adults (43 women and 33 men) between the ages of 61-67. In this experiment, the participants went through the Trier social stress test, which involved a 3-minute anticipation period and a 10-minute test period. In the Trier social stress test, participants pretend to be at a job interview and have to deliver a 5-minute free speech to convince the managers sitting in front to hire them. Those who finished early were prompted to continue, and those who finished early again were asked questions. Afterward, the participants have to complete a complex, mental math problem that is given by the managers, and about 5 minutes later, a rest period is given to end the test (Kirschbaum et al., 1993). Blood was drawn from each participant before the test, immediately after, and 90 minutes later.

The authors found that stress-associated DNA methylation changes were found in one of the two OXTR sequences that were targeted. An increase in DNA methylation was found from pre-stress to post-stress, followed by a decline in methylation (below the starting methylation

amount) from post-stress to the 90-minute recovery period. But, there was no methylation found in the BDNF sequences (Unternaehrer et al., 2012). However, because this study assesses immediate changes in methylation after psychosocial stress, this means that BDNF methylation may occur long-term, not short-term like OXTR does.

Since 2012, more studies have been done in the field of epigenetics. Scientist Helene Fachim, as well as other authors who specialize in epigenetics, conducted a study on BDNF methylation in a more long-term scenario. This study primarily focuses on BDNF methylation in psychosis patients, which can be derived from early-life stress. BDNF regulation is controlled by early-life stress, which makes it "stressor specific" (Fachim et al., 2021). They investigated whether BDNF changes were present in a first-episode of psychosis patients compared to their unaffected siblings by looking at their peripheral blood. In this study, 58 patients and 29 unaffected siblings between the ages of 16-64 completed the Childhood Trauma Questionnaire (Bernstein et al., 1994) to analyze stress measurements. DNA was gathered from human blood and 4 CpG sites were targeted. The authors found that BDNF methylation did not significantly differ between FEP patients, their unaffected siblings, and community-based influences. But, regardless of each group, higher DNA methylation was found in CpG sites 1, 2, and 3 for those who experience childhood trauma/stress (Fachim et al., 2021). The results of this study suggest that BDNF methylation is the link between early-life stress and psychosis. This data is displayed in the figure on the left. This graph displays the percentage of BDNF methylation in FEP patients, their unaffected siblings, and community-based controls based on childhood trauma/stress. In all 4 CpG sites, BDNF methylation is higher in individuals who experienced childhood trauma compared to those who did not (Fachim et al., 2021)

Along with the human study, an animal study also was conducted to analyze BDNF methylation in the prefrontal cortex and hippocampus of rats who face a mental disorder caused by early-life stress, since human brain tissue is less ethical and accessible than in animals (Fachim et al., 2021). The animal study resulted in similar findings to the human one. The rats who went through isolation (the rats with early-life stress and mental disorders) had greater BDNF methylation in both the prefrontal cortex and hippocampus compared to grouped rats, which is the control group (Fachim et al., 2021).
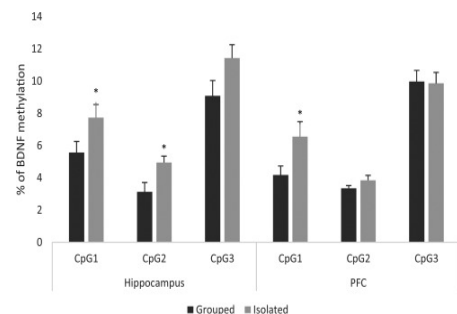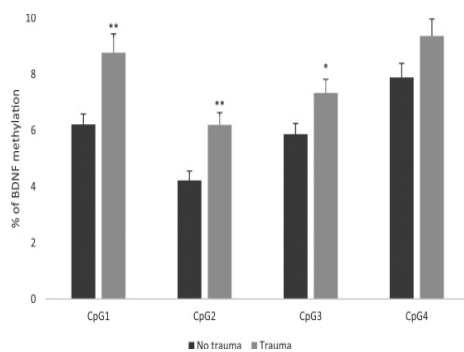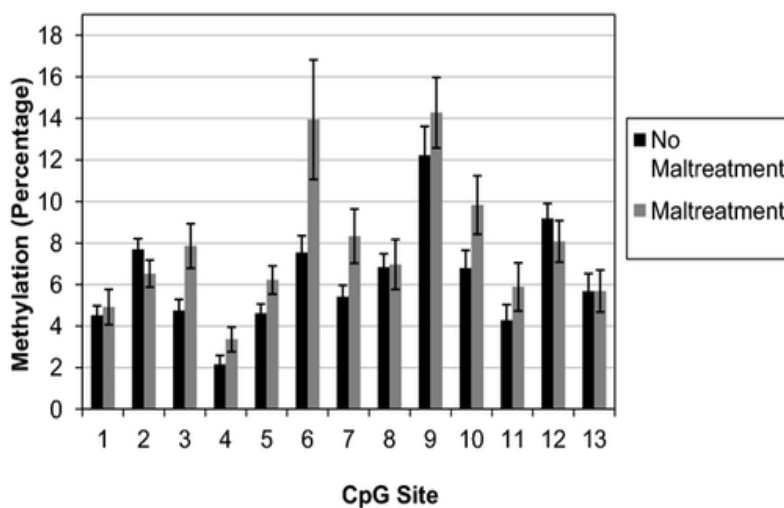
This data is shown in the graph, which displays the percentage of BDNF methylation in the two different rat groups, one in the hippocampus and the other in the PFC (prefrontal cortex). In every CpG site, except for site 3 in the PFC, methylation was higher in isolated rats than in group rats, which reflects the findings from the human study (Fachim et al., 2021).

BDNF is just one example of a stress-related gene and is not the only one that is studied. Another gene called the glucocorticoid receptor, is a significant part of stress regulation. Romens et al. (2014) studied epigenetic changes in the glucocorticoid receptor (GR) gene in 56 children (11-14 years old) in which some have experienced physical maltreatment, which is just one form of early-life stress. In this study, out of the 56 children, 18 had reports of physical maltreatment in their Child Protective Services records, while the other 38 had no records. Genomic DNA was taken from whole blood and CpG sites were identified. The authors specifically looked at 13 CpG sites in exon F_1 of the NR3C1 promoter. Children with a history of maltreatment had greater GR methylation than children who did not have a history, especially in CpG sites 3, 6, and 7, as shown in the graph below. One important point is that CpG site 3 is associated with healthy brain development, meaning that an increase or decrease in GR methylation can cause unhealthy brain development to occur (Romens et al., 2014).

The graph shows the methylation level in each CpG site for the two different groups. The greatest difference can be seen in sites 3, 6, and 7 (Romens et al., 2014).

Besides studying specific stress-related genes, scientists can also conduct longitudinal studies to analyze how stress has influenced DNA methylation over the span of someone's life, from childhood to adulthood. One longitudinal study, conducted by Essex et al. (2011) looked at how maternal and paternal stressors in the childhood of their offspring caused more DNA methylation leading into their adolescence. The study consisted of 109 children and their parents, whose stress levels were collected throughout the child's infancy and preschool years. When the children were 15 years old, DNA samples were collected. The measurements of parental stress were collected separately for each parent and fell into 5 different categories: 1 - symptoms of depression, 2 - anger expressed in the family, 3 - parenting stress, 4 - role overload, and 5 - financial stress (Essex et al., 2011). A total of 18,231 CpG sites were used in the study. The results showed that mainly maternal stress in infancy caused a DNA methylation

increase in 139 CpG sites, which is over a 5% increase from children exposed to low maternal stress. In the child's preschool years, paternal stress was most significant, causing a DNA methylation increase in 31 CpG sites. Also, these parental stressors are different among boys and girls. Paternal stress is heavily associated with girls' increase in DNA methylation while maternal stress is associated with both genders (Essex et al., 2011). Overall, this longitudinal study displayed how parental stress exposure to children causes more DNA methylation as they grow older, especially maternal stress in infancy and paternal stress in the preschool years.

Early-life stress promotes DNA methylation that can be seen in adulthood, not just adolescence, showing the long-term impact of stress. One example of this is another longitudinal study, done by Madeline B. Harms and other authors, who analyzed children who experienced early-life stress a decade later when they were in adulthood (Harms et al., 2017). 54 individuals from ages 19-23.7 agreed to participate in the study and all 54 people were a part of a previous study as children (9-13 years old) who had taken the Youth Life Stress Interview. Out of the 54 people, 29 had experienced high levels of early-life stress while the other 25 had experienced lower levels. To measure current life stress, the participants took the UCLA Life Stress Interview. DNA was taken from saliva samples and 26 methylation sites were targeted in the FKBP5 gene (Harms et al., 2017). The methylation sites were associated with childhood stress, and higher methylation sites were related to higher stress levels. Only a few sites were related to adulthood stress, but the majority are correlated with early-life stress. One methylation site, in particular, displayed a connection between early-life stress and d1PFC activation, meaning that early-life stress can cause epigenetic changes in a gene that regulates the stress response system, which can cause alterations to the prefrontal cortex function in the brain (Harms et al., 2017). Longitudinal studies can provide strong evidence to support the claim that stress and anxiety promote DNA methylation in a variety of ways, most commonly early-life stress because adolescents are studied in their childhood and adulthood, showing the long-term impact that DNA methylation has on their life as a result of early-life stress.

Early-life stress can form as a result of a variety of childhood experiences, including physical maltreatment, abuse, or neglect. A handful of studies show that early-life stress influences DNA methylation, but what if different early-life stress experiences cause different impacts on DNA methylation? Catale et al. (2020) have explored this question. They created a mice study where two groups experienced different early-life stress situations, with one group being exposed to social isolation and the other to social stress. When the mice reached adulthood, their brain tissue was extracted, along with their genomic DNA and blood. Multiple areas of the mice's brain were analyzed, including the amygdala, hippocampus, striatum, and nucleus accumbens (Catale et al., 2020). There were increased DNA methylation levels in the striatum of the social isolation mice compared to social stress mice or control mice. In the hippocampus, higher methylation was found in the social isolation mice compared to the social stress mice but was only slightly higher in comparison to the control mice. A similar trend was seen in the amygdala, though no significant differences, and no changes were seen in the nucleus

accumbens. These increased methylation levels in the social isolation mice suggest that negative regulation in the brain can occur (Catale et al., 2020).

A human study was also done to analyze the differences between childhood abuse and neglect in terms of DNA methylation. There were two clinical groups and one control group. The first clinical group was made up of 30 people who have major depression (MDD). The second clinical group was made up of 28 people who have cocaine use disorder (CUD), while the control group was made up of 32 volunteers with no mental health history. The Childhood Trauma Questionnaire was used to identify childhood neglect and abuse in the entire sample, and blood was taken from each person (Catale et al., 2020). The authors examined the blood DNA methylation in the participants and found significantly lower methylation levels in MDD participants compared to the CUD and control group participants. Overall, using the results from both studies, the authors believe that different early-life stress experiences can cause different impacts on DNA methylation and how it is expressed.

Adolescent studies are commonly used in analyzing early-life stress, but it is also important to examine neonatal periods. Time periods before adolescent years can also be a root cause for early-life stress. Fitzgerald et al. (2021) designed an animal (non-human) model study in which they created modified maternal separation (MMS) in neonatal mice, which is the most common model of early-life stress. These pups were separated from their mothers for over 3 hours a day, 10 days straight, only allowing brief interactions between the pups and their mothers. There were three groups in total: one control group and two experimental. One experimental group was decapitated at the end so that their blood and brains could be extracted and analyzed. The other experimental group was used for behavioral analysis, such as putting them in mazes (Fitzgerald et al., 2021). The authors found that early-life stress is associated with significant changes in the hypothalamic (brain) DNA methylome as well as adult behavior changes induced by stress. These methylated DNA sites were produced immediately from MMS but there was no gene expression as a result. The hypothalamus plays an important role in HPA axis regulation and any DNA methylation to it has the potential to impact brain development, which in turn can allow for stress-induced hyperactivity or diseases in adulthood.

So far, most of these studies suggest or hypothesize how an increase in DNA methylation results from stress and anxiety, but the opposite can happen as well, such that stress and anxiety do not promote DNA methylation. This can negatively impact the individual because less methylation can allow for a specific gene to be expressed more than usual. A rodent study done by Yonghe Wu and other authors analyzed how early-life stress reduces DNA methylation, which causes levels of the Pomc gene in mice to increase (Wu et al., 2014). The pituitary proopiomelanocortin (Pomc) gene is a significant mediator of stress response. Pregnant mice were gathered for this study, some being assigned as the control group and the rest as the early-life stress group. Once the pups were born, the experimental group were separated from their mothers in order to cause maternal separation stress in the male pups. After 21 days, tail blood samples were taken from the mice.

The results showed that early-life stress mice have an increase in Pomc expression in comparison to the control group based on an increase in basal plasma ACTH (adrenocorticotropic hormone) levels in the early-life stress mice. The increase in Pomc expression resulted from the decrease in DNA methylation. In the distal promoter region, there was a decrease in methylation between 15.8-38% (Wu et al., 2014). Also, the authors found that there is an age-related decrease in DNA methylation. In the control mice group, the DNA methylation percentages changed from 60% at 6 weeks old to 30% at 1 year. In the early-life stress mice, this decrease happened earlier in age, which led to an increase in Pomc expression. Besides the change in DNA methylation, early-life stress mice also face long-lasting alterations in the HPA axis activity (Wu et al., 2014). Overall, because of the decrease in DNA methylation and lack of stress regulation, the Pomc levels increase which has the potential to cause a higher stress response. So even though this study suggests that stress and anxiety do not promote DNA methylation, the lack of regulation has similar results to studies that show an increase in methylation.

Besides examining early-life stress in neonatal periods, early-life stress can also be studied in prenatal time periods through maternal perceived stress. The stress exposure by a mother to her child throughout pregnancy has the potential to cause behavioral or psychological issues in that child. Polinski et al. (2022) analyzed if maternal stress prior to and during pregnancy can cause DNA methylation in the child. An average of 2 months before pregnancy, the participants were asked to keep track of their stress levels daily on a scale from 0-3 in a journal. They continued this journal throughout their early pregnancy, eventually switching to a questionnaire for the rest of their pregnancy, ranking their stress from 0-10. DNA was taken from cord blood to analyze for methylation. These women recorded little to no stress during periconception as well as early pregnancy and moderate stress during their second/third trimester (Polinski et al., 2022).

When analyzed both separately and combined, the two different stresses were not associated with any DNA methylation changes. There were also no links between methylation to stress exposure in the fetus. However, the authors state that epigenetic mechanisms can be tissue-specific, meaning that DNA methylation changes could be found in the tissue of the fetus instead of cord blood (Polinski et al., 2022). Also, they said that the influence of a mother's early-life stress has the potential to be more impactful on the fetus than maternal perceived stress. A longitudinal study of the mother could be useful in analyzing DNA methylation changes. The authors could have also included paternal stress to see if that has any influence on the genes of the offspring (Polinski et al., 2022). Overall, there are a variety of studies in this field similar to this one where no DNA methylation is found as a result of stress and anxiety.

Limitations and Future Directions of the Epigenetics Field

Based on all of the studies that were discussed, the biggest limitation is rodent versus human studies. Many rodent studies are conducted instead of human ones due to the fact that most of the analysis methods are considered unethical and inaccessible in humans (Romens et

al., 2014). For instance, when analyzing brain methylation, those brain tissues and the brain itself must be looked at. The main way to do this is to decapitate the organism, which is what researchers do to rodents in this scenario. In humans, blood is typically assessed for methylation, though looking at specific tissues could be more accurate (Polinski et al., 2022). Developing noninvasive or minimally invasive ways to access tissues in humans can be done in the future to gain more accurate results. It is also important to note that some experiments do not have control groups. However, in this field, there should be control groups because a variety of environmental and outside factors can easily influence the findings of the study, meaning that the results do not always come from stress and anxiety alone. Also, DNA methylation changes are not permanent and can be reversed (Romens et al., 2014). In the future, experts can study how to intervene and reverse DNA methylation as a result of stress and anxiety in children. These interventions can help lessen exposure to the consequences of early-life stress or mediate its effects in later adulthood. Future advancements in this field can help researchers start identifying solutions rather than continue to analyze the problem.

Conclusion

The field of epigenetics has become more popular in recent years and is widely studied. DNA methylation, one of the most common forms of epigenetics, is mainly analyzed in relation to behavioral or mental health issues. With the wide variety of studies discussed in this paper, mental health, such as stress, can heavily influence DNA methylation, which in turn can cause gene expression. But, the opposite has been looked at as well, such that stress and anxiety don't promote DNA methylation, or it could also cause a decrease in methylation to occur. There are negative consequences associated with stress and anxiety that form through DNA methylation, such as impacted brain development or the likelihood of developing physical diseases. Mental health has become a significant topic in today's society, just like epigenetics has become significant in molecular biology. By studying the relationship between the two, experts can find the answers to many questions about the link between genotype and phenotype, or in other words mental health and physical health. With more advancements in the future, these newly-founded answers can form solutions to these problems that can help the lives of many people around the world.

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How can the CRISPR system be utilized as an innovative approach to combat antibiotic resistance by specifically targeting efflux pumps in bacteria? By Aishani Chikkareddy and Robert Melde

Abstract

Antibiotic resistance has become a significant threat to global public health, rendering conventional treatments ineffective against bacterial infections. Efflux pumps, which actively expel antibiotics from bacterial cells, play a pivotal role in mediating this resistance. This review paper aims to explore the viability of utilizing CRISPR/Cas9 to disrupt efflux pumps in bacterial pathogens, potentially controlling antibiotic resistance. Here, we critically evaluate the current state of knowledge and future prospects of antibiotic resistance stemming from efflux pumps. Precision gene editing plays a novel role in the fight against antibiotic-resistant bacteria. Here we review three different studies investigating the use of CRISPR in bacteria and its relation to efflux pumps. Two of the papers will investigate how CRISPR/cas9 or CRISPRi can be used to lessen the effects of efflux pumps, and one of the papers will look at the natural CRISPR system in bacteria and how it affects antibiotic resistance. Ultimately, this research paper aims to offer valuable insights and promote innovative strategies to effectively mitigate the global prevalent threat of antibiotic resistance.

Introduction

The antibiotic resistance crisis is a growing global concern that arises from the overuse and misuse of antibiotics, leading to the development of bacteria that are resistant to these drugs. (McAdam et al. 2012) Antibiotics are essential in treating bacterial infections and have been pivotal in modern medicine, saving countless lives since their discovery. However, the misuse of antibiotics in both human and animal health and agriculture has accelerated the emergence of antibiotic-resistant bacteria, often called "superbugs." The emergence of superbugs, limited treatment options available, the global health impact, economic consequences, and the ineffectiveness of current antibiotics all make this problem very prevalent and dangerous to society. Proteins called efflux pumps in bacteria are a significant contributor to the increasing problem of antibiotic resistance. (Sharma et al., 2019). Efflux pumps are specialized proteins located in the cell membranes of various organisms that actively transport a diverse range of substances, including toxins, drugs, and potentially harmful compounds, from inside the cell to the external environment. Efflux pump activity is significantly correlated with antibiotic resistance in bacteria. (Du et al., 2018). Research on efflux pumps has been conducted across various bacterial species, each focusing on distinct aspects of antibiotic resistance. However, a comprehensive examination of the potential applications of CRISPR/Cas-9 in addressing efflux pump-related challenges in many bacterial species is absent from the current literature. Here we will review recent case studies that employ CRISPR/Cas9 technology to target efflux pumps as a means of studying antibiotic-resistant bacteria. This paper will encompass a diverse range of bacterial species to offer a holistic perspective on this innovative approach.

Efflux Pumps

At its core, antibiotic resistance refers to the ability of bacteria to withstand the effects of antibiotics, rendering these drugs ineffective. Bacterial antibiotics work by blocking crucial cellular processes in bacteria and triggering cellular responses that lead to bacterial cell death (Kohanksi et al., 2010). This phenomenon arises due to one pivotal mechanism: the utilization of efflux pumps. Efflux pumps are crucial defense mechanisms employed by bacteria, enabling them to expel not only antibiotics but also a diverse array of other compounds from within the cell. This general defense mechanism makes efflux pumps a robust group of proteins for bacteria to resist numerous antibiotics, posing a significant challenge in treating infections. Efflux pumps are a highly diverse group of proteins, resulting in a wide variety of these pumps with distinct functions and substrate specificities. They are categorized into families like the Major Facilitator Superfamily (MFS), Multidrug And Toxic compound Extrusion (MATE), Small Multidrug Resistance (SMR), and ATP-Binding Cassette (ABC) based on their structure and substrate specificity. Some, like MFS and MAR, share topological similarities, while others are distinguished by sequence homology or phylogenetic differences (Chetri, 2023). Many of these efflux pumps, especially in the MFS and ABC families, confer multidrug resistance. They are capable of expelling a broad range of substances, including different classes of antibiotics and non-antibiotic drugs. The presence of efflux pumps in both prokaryotes and eukaryotes underscores an ancient evolutionary origin and highlights their cellular importance. Some pumps, like SMR, are exclusive to bacteria, while MET pumps are specific to eukaryotes. (Van Bambeke et al. 2000) Efflux pumps consist of ABC transporters, which are a diverse group of proteins responsible for the ATP-dependent import or export of various solutes. They consist of transmembrane domains (TMDs), with substrate-binding pockets and nucleotide-binding domains (NBDs) for ATP binding and hydrolysis, which drive the transport process. (Abdi et al. 2020) The two main categories of ABC exporters are homodimeric and heterodimeric exporters. Heterodimeric ABC exporters, such as PatAB, LmrCD, BmrCD, and EfrCD, are particularly relevant for antibiotic resistance in Gram-positive bacteria. While homodimeric exporters typically have two equivalent ATP-binding sites, heterodimeric exporters possess a degenerate binding site that doesn't support ATP hydrolysis. This reduced ATP hydrolysis capacity can alter the dynamics of the transport cycle, potentially enhancing resistance to antibiotics by impeding drug expulsion (Van Bambeke et al., 2000). It is essential to be able to lessen or completely eliminate the effects of efflux pumps in order to eradicate the problem of antibiotic resistance. One approach to mitigating the influence of efflux pumps involves the utilization of CRISPR-Cas9 genetic engineering technology.

CRISPR CAS-9

CRISPR/Cas9 is a groundbreaking gene-editing technology that is transforming biomedical research. It allows for the correction of genetic errors, gene regulation, and rapid gene manipulation in cells and organisms. In the laboratory, it has been successfully used to correct genetic defects in mice and human embryos, offering potential clinical applications such as gene

therapy, treating diseases like HIV, and customizing treatments for cancer. In the field of pediatrics, CRISPR/Cas9 holds promise for clinical applications, but there are ethical and safety concerns that need to be addressed. For example, there are concerns about the long-term effects of genetic modifications and the potential for unintended consequences in children. CRISPR can be implemented in molecular biology research in various ways. In the CRISPR/Cas9 system, Cas9 is an endonuclease enzyme that cuts DNA at specific target sequences guided by a customizable RNA molecule called guide RNA (sgRNA or gRNA). It is used for DNA editing and modification (Vidyasagar, 2018). Another technique, CRISPRi, uses a catalytically inactive or "dead" Cas9 (dCas9) protein. dCas9 cannot cut DNA like the active Cas9 but is used to interfere with gene expression by blocking or repressing the transcription of specific genes. The guide RNA in CRISPRi also directs dCas9 to the target gene's promoter region to achieve this repression (Jensen et al., 2021). CRISPRi is derived from the CRISPR/Cas9 system; it interferes with gene expression without making structural changes to the underlying DNA sequence. Both CRISPR/cas9 and CRISPRi are effective tools with distinct applications in genetic research and clinical potential, and they are both useful techniques to target efflux pumps.

Case studies

There are only three studies to date that have investigated using CRISPR based research to investigate the role of efflux pumps in antibiotic resistance. The first covers a CRISPRi approach in targeting the AcrAB-TolC Efflux Pump in E. coli, the second a CRISPR-Cas approach in A. baumannii, the third where researchers investigated the role of the native CRISPR-Cas system in Acinetobacter baumannii, and lastly, CRISPR-Cas9 Gene Editing in Candida albicans, which focuses on using CRISPR-Cas9 gene editing to target and disrupt genes associated with efflux pumps in the fungal pathogen Candida albicans.

In the research paper, "Engineering a CRISPR interference system targeting AcrAB-TolC efflux pump to prevent multidrug resistance development in Escherichia coli," the researchers use the bacteria Escherichia coli (E. coli), specifically the E. coli strain HB101. This strain is commonly used in laboratory research and is a well-known model organism for various genetic and molecular biology studies. The researchers use a CRISPR interference (CRISPRi) system to target the AcrAB-TolC efflux pump. They designed single-guide RNAs (sgRNAs) to target various loci involved with the AcrAB-TolC efflux pump, including AcrA, AcrB, and TolC. These sgRNAs are designed to bind to the non-template strand of the genes and interfere with their transcription, reducing the expression of the efflux pump components. In their experiments, the researchers primarily use a form of gene silencing with the CRISPRi system. Gene silencing involves reducing the expression of specific genes without making permanent changes to the DNA sequence (Wan et al., 2022). In this case, the sgRNAs are guiding the Cas9 protein to bind to the target genes' promoter regions, preventing their transcription and thereby reducing the expression of the AcrAB-TolC efflux pump components. This is a reversible and temporary method of gene regulation, as it does not alter the underlying DNA sequence. The protein-coding regions of the genome are primarily being targeted with the researchers' CRISPRi system. Specifically, they designed sgRNAs to bind to the non-template strands of the coding sequences

(CDs) of the AcrA, AcrB, and TolC genes. By targeting the CDs, they aim to interfere with the transcription of these genes and reduce the expression of the corresponding proteins that make up the AcrAB-TolC efflux pump. The effectiveness of the CRISPRi method varied depending on the specific sgRNAs used and the target genes. The sgRNAs designed to target AcrA, AcrB, and TolC were effective in reducing the transcription of these genes, with varying degrees of inhibition. The most effective sgRNA cluster, acrB1tolC2, resulted in a significant reduction in the transcription of all three genes (AcrA, AcrB, and TolC). They found that the CRISPRi system, which used sgRNAs, is much more effective in regulating the AcrAB-TolC efflux pump by targeting acrA, acrB, and tolC than a previous study that used sRNAs (small regulatory RNAs)(Wan et al., 2022). This reduction in gene expression correlated with increased susceptibility to multiple antibiotics, such as rifampicin, erythromycin, and tetracycline. Additionally, the CRISPRi system reduced biofilm formation in E. coli HB101. Overall, the study demonstrated that a CRISPRi-based approach targeting the AcrAB-TolC efflux pump could serve as a novel approach to treating antibiotic-resistant *E. coli* infections.

The next study I reviewed was "CRISPR-Cas in Acinetobacter baumannii Contributes to Antibiotic Susceptibility by Targeting Endogenous AbaI ."In this paper, the researchers highlight the connection between the natural CRISPR-Cas system and antibiotic resistance in A. baumannii. They found that deleting any component of the CRISPR-Cas system led to increased antibiotic resistance because the CRISPR-Cas system was found to repress multidrug efflux pumps. Deletion of the system led to increased efflux pump activity, which is associated with antibiotic resistance. The researchers chose to study Acinetobacter baumannii, which is a multidrug-resistant bacterium that poses challenges in clinical anti-infective treatments. This bacterium can acquire multidrug resistance through various mechanisms, including horizontal gene transfer and mutations (Wang et al., 2022). It can survive in various environments and is a significant public health concern. CRISPR-Cas systems are classified into various types (I-VI) and subtypes. Type I-Fb CRISPR-Cas system is prevalent in A. baumannii and consists of specific Cas proteins and CRISPR arrays. The researchers investigate how the Type I-Fb CRISPR-Cas system in A. baumannii affects quorum sensing (which is how the bacteria communicate with each other via signaling molecules) and antibiotic resistance. The study focused on a clinical isolate called AB43, which possesses a complete I-Fb CRISPR-Cas system. They found that the Cas3 nuclease of the Type I-Fb CRISPR-Cas system in AB43 regulates quorum sensing. Specifically, it reduces the synthesis of the quorum sensing regulator abaI mRNA.This reduction leads to decreased efflux pump activity, weaker biofilm formation, increased production of reactive oxygen species (ROS), and decreased drug resistance (Wang et al., 2022). The study analyzed a collection of clinical A. baumannii isolates and found that most isolates with incomplete or no CRISPR-Cas systems were multidrug-resistant. This study highlights the crucial role of the CRISPR-Cas system in mediating antibiotic susceptibility in *Acinetobacter baumannii*. By regulating quorum sensing and efflux pump activity, the CRISPR-Cas system inadvertently affects the bacterium's ability to resist antibiotics. These findings offer new insights into the complex mechanisms behind antibiotic resistance in *A.*

baumannii. The use of synthetic CRISPRi or CRISPR/Cas9 approaches to target the natural CRISPR-Cas system could become a viable approach to combat the growing issue of multidrug resistance in this clinically significant bacterium.

The last paper I reviewed was "A CRISPR–Cas9-based gene drive platform for genetic interaction analysis in Candida albicans".The paper focuses on the genetic manipulation of the fungal pathogen Candida albicans, a leading cause of infection in immunocompromised individuals. It presents treatment challenges due to its close evolutionary relationship with humans, leading to limited non-toxic antifungal agents. Their study investigates efflux pump mutants in *C. albicans* and their role in mediating susceptibility to antifungal stress, particularly to fluconazole. Fluconazole holds significant importance in the treatment of fungal infections, particularly those caused by *Candida albicans*. They discovered that mutations in efflux pump genes, notably CDR11, significantly affected the organism's sensitivity to fluconazole. (Shapiro et al., 2018). The researchers then developed a GDA platform using CRISPR-Cas9 technology. *Candida albicans* is a diploid organism, meaning it has two copies of each gene. So, traditional methods of genetic manipulation can be inefficient in diploids since altering both gene copies to study gene function is complex and time-consuming. The GDA platform simplifies this process. Also, In the context of antifungal and antibiotic resistance, the GDA platform allows researchers to swiftly create and study mutants lacking specific efflux pumps. Understanding how these pumps contribute to drug resistance can inform the development of more effective antifungal treatments. In their GDA system, a specially designed DNA donor molecule acts as a 'selfish' genetic element. When introduced into the organism, it not only replaces the targeted gene but also propagates itself to replace corresponding genes at other loci. Their research uncovered synthetic lethal interactions between transporters, providing insights into cellular ion homeostasis and potential therapeutic targets (Shapiro et al., 2018). The principles established in this study could be applied to other fungal pathogens, like *Candida auris*, known for multidrug resistance. Their research transforms the ability to perform genetic interaction analysis in *C. albicans*, offering insights into virulence factors and antibiotic resistance. In addition, the principles and methodologies developed could be applied to other fungal pathogens, potentially aiding in the treatment and understanding of various fungal infections.

Discussion

CRISPR can be utilized and studied in numerous facets as a tool to combat antibiotic resistance in microbes.

The first paper, which focuses on E. coli, demonstrates the successful use of CRISPR interference (CRISPRi) to target the AcrAB-TolC efflux pump components. The effectiveness of this approach varies depending on the specific single-guide RNAs (sgRNAs) used, with the most effective sgRNA cluster (acrB1tolC2) resulting in a significant reduction in the transcription of the targeted genes. This reduction in gene expression is correlated with increased susceptibility to multiple antibiotics, highlighting the potential for CRISPRi to combat multidrug resistance in E. coli.

In contrast, the second paper examines Acinetobacter baumannii, a multidrug-resistant bacterium. This paper is very different from the other two. While the other two papers use the CRISPR genetic engineering technology to go in and make edits, this paper investigates what happens if we turn off the natural CRISPR system in the bacteria, revealing the importance of CRISPR. The researchers found that deleting any component of the CRISPR-Cas system in A. baumannii actually leads to increased antibiotic resistance due to increased efflux pump activity. This finding emphasizes the role of the CRISPR-Cas system in repressing efflux pumps, and its deletion results in higher antibiotic resistance. The study also identifies the regulatory role of the Cas3 nuclease in quorum sensing and its impact on antibiotic resistance.

The third paper focuses on Candida albicans, a fungal pathogen, and its efflux pumps. This research paper introduces an innovative CRISPR-Cas9-based Gene Drive Array (GDA) platform specifically tailored for the genetic analysis of *Candida albicans*, which enables the efficient creation of homozygous double-deletion mutants by using a modified DNA donor molecule that acts as a 'selfish' genetic element. It replaces targeted genes and propagates to replace corresponding genes at other loci. The study focuses on dissecting the roles of efflux pump genes in antifungal resistance, especially towards fluconazole, revealing specific genes like CDR11 that significantly impact the pathogen's drug sensitivity. Additionally, the research delves into adhesin genes critical for biofilm formation, a key factor in *C. albicans'* pathogenicity. Through high-throughput screening and comprehensive genetic interaction analysis, the researchers identify crucial virulence regulators and how these genetic networks adapt under various environmental stressors, including antifungal treatments. Their research marks a significant advancement in the field of fungal genetics, antibiotic resistance, and infectious disease research.

While CRISPR technology shows promise in combating antibiotic resistance, its effectiveness can vary due to many factors. The differences in the bacterial species themselves could contribute to variations in antibiotic resistance levels. A. baumannii, for instance, is notorious for its intrinsic and acquired antibiotic resistance mechanisms, often making it more resistant to antibiotics compared to E. coli or Candida albicans. The natural variation in antibiotic resistance among these species may explain some differences in the extent to which CRISPR-based interventions affected resistance levels. The variability in outcomes across these studies could also be attributed to the selection of specific genes or loci as targets for CRISPR-based interventions. Some genes may have a greater influence on antibiotic resistance, while others may have smaller or more nuanced effects. For example, In the E. coli study, the researchers designed single-guide RNAs (sgRNAs) to target components of the AcrAB-TolC efflux pump, including AcrA, AcrB, and TolC. The effectiveness of the CRISPR interference (CRISPRi) method varied depending on the specific sgRNAs used and the target genes. For instance, the sgRNA cluster acrB1tolC2 was highly effective in reducing the transcription of all three genes (AcrA, AcrB, and TolC), resulting in a significant reduction in antibiotic resistance. On the other hand, some sgRNAs may have had lesser effects on specific target genes. In the A. baumannii research, the focus was on the Type I-Fb CRISPR-Cas system's impact on quorum sensing and antibiotic resistance. Deletion of its components boosted antibiotic resistance

through increased efflux pump activity. This implies multiple CRISPR-Cas genes collectively influence antibiotic resistance

Overall, these papers showcase the versatility of CRISPR technology in addressing antibiotic resistance. They demonstrate its potential to reduce antibiotic resistance in different bacterial species through various strategies, including gene silencing (CRISPRi), regulatory role modulation (Cas3 nuclease), and precise gene editing (CRISPR-Cas9). The varying effectiveness of these methods across different organisms and targeted mechanisms emphasizes the need for tailored approaches in combating antibiotic resistance. The findings from these studies not only advance our understanding of the genetic foundations of antibiotic resistance but also open avenues for developing more effective treatments against resistant strains of bacteria and fungi. As we continue to explore the capabilities of CRISPR technology, it is important to consider the specificities of each organism and the ethical implications of genetic manipulation, ensuring that these powerful tools are used responsibly and effectively in the ongoing battle against antibiotic resistance.

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An Exploration of Advocacy Movements: Destigmatizing HIV/AIDS for Women in Africa
By Alexis Park

Abstract

Since the beginning of the epidemic, approximately 86 million people have become infected with the Human Immunodeficiency Virus (HIV). However, the stigma and discrimination of individuals living with HIV have made HIV a nuanced public health issue. Today, heterosexual transmission remains the dominant mode of transmission. It accounts for about 85% of all HIV-1 infections, and women currently make up about 42% of those infected with HIV worldwide, with over 70% of the population living in sub-Saharan Africa (Simon et al). Due to the additional implications for mother-to-child transmission, stigma against women living with HIV (WLWH) has reduced the quality or limited access to medical and social care for women. It has led to high mortality rates and numbers of children born HIV-positive. The efforts of activism in improving policy protection that reduces societal and medical stigma around HIV and promotes HIV education have been shown to significantly improve the quality of care that women who are HIV-positive receive. This paper will explore historical and modern advocacy movements and their impact on HIV stigma and care in Africa through a literature review. This study highlights the gender disparity and political foundation of the global HIV epidemic to provide a basis for future studies and interventions on this critical issue for aiding future generations of women.

Introduction

HIV, or human immunodeficiency virus, attacks the cells that aid the body in fighting infection and is spread by contact with bodily fluids, mostly during unprotected sex or through sharing injection drug equipment (HIV.gov). HIV, when left untreated, can progress to a disease known as AIDS or acquired immunodeficiency syndrome. There are two types of HIV: HIV-1, known for affecting populations globally, and HIV-2, which is almost exclusive to West Africa.HIV-1 is known to be more potent than HIV-2, as it progresses more rapidly to AIDS than HIV-2, and can also be transmitted more easily (Alamenda County Public Health Department). HIV-1 was first identified as a causative organism of the AIDS disease in the USA in 1983, and HIV-2 was reported first in Africa in 1985 (Bhatti et al.).

By the end of 2017, 36.9 million people were living with HIV worldwide, with 1.8 million new infection cases and 940,000 deaths. There is currently no region of the world untouched by the HIV pandemic. Those infected by HIV may develop flu-like symptoms but must be tested for HIV to be diagnosed. Although the presence of HIV and AIDS as a disease was recognized due to an increase in infection and cancer among homosexual men, heterosexual transmission is the dominant mode of transmission and accounts for about 85% of all HIV-1 infections (Bekker and Beyre). With the expansion of HIV as an epidemic, the treatment in HIV and AIDS care has also evolved, especially with advances in Antiretroviral therapies (ART). ART is recommended for all patients to slow the progression of HIV to AIDS and is known as

the most effective management of HIV infection possible. This method of treatment utilizes different combinations of available drugs as the Standard ART consists of a concoction of at least three medicines that control the multiplication of HIV in infected patients and increase the count of CD4 cells. This concoction thus prolongs the asymptomatic phase of infection, slowing the progression of the disease, and also helps in reducing the risk of transmission (Bhatti et al.).

The scientific community first recognized AIDS as an actual disease following an increase in the incidence of sporadic opportunistic infections and cancers among otherwise healthy homosexual men.

With this discovery of HIV and AIDS in correlation with LGBT individuals, the increase of social stigma and discrimination has permeated the social culture around the disease. Although the advancements in HIV treatment and public understanding have progressed to a great extent, studies have recorded that stigma and discrimination have not only fueled the spread of the epidemic but have hurt patients through experiences of social isolation, stress, emotional coping, and the denial of social and economic resources, hindering the progress of HIV/AIDS treatment (Tran et al.). The presence of this discrimination ranges from interpersonal, community, and healthcare environments, even in the most developed countries. Most prominently, the presence of this discrimination in healthcare is portrayed through unconsented HIV testing, the refusal to give treatment to a patient, and confidentiality violations, especially within healthcare (Tran et al.).

HIV Stigma among Women Globally and in Africa

Studies have shown that stigmatizing beliefs against HIV and AIDS have prevented people from getting tested for HIV, receiving and staying in care, and correctly administering HIV drugs (The Well Project). However, as a woman with HIV or AIDS, these stigmas are exacerbated by social and structural biases that are implicated regularly against women. Over 30% of women worldwide have experienced rape, physical violence, or stalking by an intimate partner in their lifetime, and these statistics applied to women

living with HIV (WLWH) leads to a greater likelihood of women being blamed for their HIV status and or facing violence in domestic settings (World Health Organization). The systemic oppression and position in society of women that lead to such issues have placed additional restrictions and both external and internal stigma in HIV/AIDS care (Appiah et al.).

Women living with HIV (WLWH) experience higher rates of posttraumatic stress, depression, and anxiety than their male counterparts. Not only do these mental health issues affect the well-being and quality of life of these women, but they act as another barrier to addressing these concerns and providing treatment. Women living with HIV have been historically under-treated for mental health concerns, despite concerns regarding intimate partner violence, inconsistent condom use, and history of other sexually transmitted infections exacerbate these conditions (Waldron et al.). After HIV diagnosis, women experience more than 3 times as many mental health issues. This statistic can be aggravated by gender, race/ethnicity, poverty, and intersectional disparities.

Adverse mental health issues WLWH experience are linked to worse HIV-related health outcomes, especially as studies have shown to be inconsistent in providing care as an option to these individuals at all. However, to address mental health disparities with WLWH that have been linked with ART adherence and worse disease progression, sexual health interventions have incorporated psychosocial aspects such as cognitive reappraisal and stress management to address these disparities (Lechner et al.).

Even in the United States, a first-world country, the criminalization of HIV exists within more than half of United States jurisdictions. However, little evidence supports the effectiveness of HIV prevention these laws, and they are suspected of undermining prevention efforts in the US National HIV/AIDS Strategy in stigma and care. Current HIV-specific laws establish that HIV status increases the severity of an existing crime and can also distinguish an act from legal behavior. For example, consensual sex can be classified as an illegal activity if one's HIV status is unknown and results in large punishments for existing crimes (Lazzarini and Galletly). While the argument that these HIV laws are protecting women against men and HIV exposure must be considered, criminalization also includes laws discriminatory to women. Through some state health departments, WLWH are required to sign agreements that they will be guilty of a felony if they ever have unprotected sex or if they get pregnant (U.S. Equal Employment Opportunity Commission).

It is also important to note that these policies do not reflect scientific progression in the field of HIV. Scientists have established, since the dawn of HIV restriction and law, that the impact of antiretroviral therapy, the risk of HIV transmission, and the diagnosis of viral strains is immense. However, these policy restrictions do not reflect these advancements despite these laws being intended to be effective in reducing HIV deterrence. Findings from empirical studies on the impact of these laws suggest that these laws do not decrease HIV infections or pose any other positive public health impacts, instead directing further hatred and discrimination toward homosexual communities. Additionally, women, who can risk passing on HIV to their children if pregnant when being unable to access proper care, can be susceptible to these charges, especially regarding inconsistent abortion policies (McQuillan et al.).

Additionally, due to inequitable distributions of resources and ecological challenges, poverty is one of the leading factors in both policy inequities and general HIV inequities (Webel). Traditional gender roles that restrict women from education and personal finances cause them to be generally more impoverished than their male counterparts. Living in chronic poverty, where women have little control and fewer choices to earn money or keep a job, often leads to women needing to trade sex for housing, food, and money (Adimora and Schoenbach). For instance, a recent study in Washington, DC, found that the increased risk for HIV infection in the African-American/Black female community is related to social networks rather than to individual risk factors (Magnus).

HIV inequities differ on a global scale. In the United States, the Centers for Disease Control and Prevention estimated a 12% decline in new HIV infections from 2017 to 2021. Acquired HIV rates among women through heterosexual contact decreased by 16% (5,100 out of

32,100 individuals) as of 2023 (HIV.gov). The number of women with HIV is currently 23% of the 1.1 million people in the United States (KFF). In stark contrast to America, HIV statistics in sub-Saharan Africa reflect the poor economic health and social disparities of the region. The mortality rates caused by HIV in developing countries are attributed to food insecurity and malnutrition, although there is currently no cure for HIV itself. A study by the United Nations (UNAIDS) reported that women and girls continue to carry the heaviest HIV burden in sub-Saharan Africa: 25% of the HIV infections in 2020 were adolescent girls aged 15-24 years old, and in total, 63% of new HIV infections were women (UNAIDS). Sub-Saharan Africa's economic growth has historically been low, dipping to 3.6% in 2022 from 4.1% in 2021 and being projected to drop 3.1% in 2023 (The World Bank in Africa). Additionally, human development in this region has been steadily improving but has recently plateaued after achieving a score of 0.55 on the Human Development Index (HDI) in 2021. A score of 0.55 is at the cusp of "low" development but is classified as being "medium" development (Human Development Reports). This score still represents a low level of human development based on economic and non-economic factors, and has remained within the indicative index scores of 0.42 and 0.56 (Sasu).

A growing body of evidence suggests that both income and gender-based inequalities can impede economic growth, and the gender inequality index (GII) of sub-Saharan Africa reads below the average GII, indicating that sub-Saharan Africa is low-performing in bridging gender inequities. The GII "captures gender inequality in health (maternal mortality ratio and adolescent fertility rate), empowerment (gap in secondary education and share of parliamentary seats) and economic participation (gap in labor force participation rates)" (Hakura and Hussain). In Africa, roles and responsibilities continue to be gendered. While both women and men in Africa are responsible for productive work, women are additionally held to the responsibility of assuming a majority of reproductive and domestic work (Kiptot). As men took a head role in these households, many women have experienced normalized intimate partner violence. A review demonstrated that both sexes justified such violence if a woman burned food, neglected her children, argued with her husband or insulted him, or accused her partner of infidelity (Waltermaurer). In a publication from 2016, it was estimated that physical or sexual intimate partner violence ranged from 11.5% in Burkina Faso, 25.9% in Ivory Coast, 33.1% in Mozambique, and up to 35.2% in Zimbabwe (McSwine). These high rates of violence against women and young girls can impede both personal health and socioeconomic development, especially with child brides. Additionally, women who experience intimate partner violence are more at risk of having poor pregnancy outcomes and contracting sexually transmitted infections such as HIV (McSwine).

In general, women in Africa are especially vulnerable to HIV infection due to both biological susceptibility and men's sexual power and privilege. In sub-Saharan Africa, HIV has been transmitted in 80% of cases as a result of heterosexual activity, and existing gender disparities create a basis for an unsafe environment for WLWH to receive information, care, and support (Hunter). A lack of general and sexual education and therefore, a dependence on a male

partner for economic or social support largely contribute to the potential of abuse and violence in the relationship. Although in heterosexual relationships, sexually transmitted infections may be passed on by a man's opposition to condoms and sexual dominance, the woman may bear the blame for spreading the disease, regardless of the circumstances (PRB).

Stigma against people with HIV/AIDS in Africa can lead to community ostracization, employer discrimination, and violence. Such discrimination has largely accompanied an individual's public disclosure of having this disease. This is most prominently demonstrated by the killing of Gugu Dlamini, who was stoned to death by the Kwazulu Natal community in 1997 after publicly disclosing her HIV status (Mavhunga). The stigma associated with HIV/AIDS has historically caused individuals to deny their personal risks of infection, avoid being tested, or hide their infection - all without seeking support and proper treatment (Kang'ethe). Gender roles, abusive and unsafe situations, and HIV stigma contribute to high numbers of HIV/AIDS infections and mortality in women and can be passed onto children if the WLWH is pregnant (Kapoor).

Outside of sub-Saharan Africa, over 70% of new HIV infections in 2022 were among men and boys. However, within sub-Saharan Africa, women accounted for more than 63% of new infections (Office on Women's Health). The statistics around HIV with women in Africa shocked government officials and activists, especially given that girls and women made up more than half of the 37.7 million people living with HIV in 2022 (UNAIDS). Although the rates at which WLWH have been infected have improved significantly throughout history, it is imperative for us to recognize these efforts as we continue to address the diverse issue of women's needs and HIV diagnoses in future responses.

Historical Movements and Advocacy (1980-2019)

As HIV/AIDS grew to be one of the most significant pandemics in history, advocacy groups and movements have been at the forefront of fighting for greater access, care, and destigmatization of the disease. As the epidemic expanded into developing countries, countries united globally to address this disease. However, as HIV/AIDS is widely known as a disease that significantly affects LGBTQ+ individuals, activists have faced challenges due to discrimination.

The Centers for Disease Control and Prevention (CDC) was the entity initially assigned to determine the AIDS outbreak. Investigators inquired into the epidemic through case surveillance, identifying risk groups as men who have sex with men (MSM) and injection drug users (IDU) (De Cock et al.).Transmission was sexually linked, reproductively linked through mother to child, and additionally traced through blood exposures and transfusions. This led the FDA to restrict blood donation from MSM and went on to institute a lifetime ban on blood donation from LGBTQ + individuals and women who have had sex with MSM. The intent behind the ban was to maintain a safe blood supply as a high public health priority, but this ban further perpetuated the stigma against members of the LGBTQIA+ community (Mann and Anderson).

As mortality and infection rates rose, international efforts united to combat HIV. In the first decade of the epidemic, the World Health Organization (WHO) mainly drove these endeavors through its Global Programme on AIDS in 1987. The program recommended a combination prevention approach that is tailored to the population and reflects the epidemiology of the setting. Sites utilize WHO guidance and resources by the five preventions pillar, which includes condom accessibility, pre-exposure prophylaxis (PrEP), and voluntary medical male circumcision (VMMC) (World Health Organization). By organizing WHO guidance and resources through the five prevention pillars, WHO has supported the prevention of HIV and other sexually transmitted infections, testing, and treatment to not only meet the needs of infected individuals but also reduce new infections.

Further global initiatives since 1987 include the Joint United Nations Programme on HIV/AIDS (UNAIDS, 1996) and the Global Fund to Fight Aids, Tuberculosis, and Malaria, which were formed to coordinate worldwide attention to the epidemic or finance developing countries. Africa has historically received the majority of this funding, receiving 7.695 million in U.S. dollars in this recent 2023-25 cycle (The Global Fund). The structural inequities within Africa have deterred global efforts, as low development in poverty and social-cultural aspects favor the spread of HIV/AIDS. South Africa has been, and continues to be, most prominently in need, as it has the highest population of individuals with HIV, with almost 4.2 million people as of 2000.

East and Central Africa have had lower prevalence rates of HIV/AIDS and have seen extensive improvement, especially in Uganda. Uganda's success was highly attributed to the high-level support that the head of state, President Yoweri Museveni, provided through a multi-sectoral approach from 1986. In face-to-face interactions with Ugandans at all levels, he emphasized that fighting AIDS was a "patriotic duty" requiring openness, communication, and strong leadership from the village level to the State House (Green). Addressing the threat of HIV/AIDS encouraged constant, candid national media coverage of the epidemic, and the country has maintained a National AIDS Control Program (ACP) and a national sentinel surveillance system, which has tracked the epidemic since 1987 (McSwine).

However, within South Africa, such governmental support was lacking during the pitvotal time of the epidemic. AIDS emerged in South Africa in 1982, introduced through shocking headlines that announced the arrival of the 'homosexual disease' or the 'gay plague.' (Mbali). The issue of HIV/AIDS, while being potent before either presidency, became most prominent during Nelson Mandela's (1994-1999) and Thabo Mbeki's (1999-2004) tenures.

By 1990, when Mandela was released from prison, nearly 1 percent of South African adults were already HIV-positive (Breslow). By 1994, the epidemic was taking greater control of South Africa. With prevalence climbing amongst women, AIDS was massively established as a heterosexually transmitted disease as well. While activists, one of which being Justice Edwin Cameron, a judge on the Constitutional Court of South Africa and a gay rights activist, hoped that Mandela would aid the movement during his time in office, there were also other priorities in play that obstructed such progress. Mandela, being the first black president of South Africa

during a time of military and political instability, mainly focused on dismantling apartheid and constitutional reform throughout his presidency, which began in 1994. Additionally, while there was consensus on the importance of HIV within the African National Congress (ANC), there was widespread involuntary denial of the epidemic. Fear of HIV/AIDS only heightened due to a lack of political leadership from Mandela. When Thabo Mbeki came into office in 1999, his active denialism of the disease only exacerbated public opinion.

Mandela's activism during HIV/AIDS, however, was not nonexistent but delayed. He acted as an advocate for HIV/AIDS following his presidency, especially during the time of widespread induced denialism from Thabo Mbeki. In 2000, Mandela closed the 13th International AIDS Conference, saying that poor people in Africa, "who would carry a disproportionate burden of the AIDS epidemic," would wish that "the dispute about the primacy of politics or science be put on the back burner and that we proceed to address the needs and concerns of those suffering and dying" (Sidley). This proclamation acted in contrast to Mbeki, who had expressed doubt over the etiology of AIDS while opening the conference, instead alluding the severity of the disease to extreme poverty (Mbeki). While tension between the party ranks between Mbeki and Mandela simmered, Mandela's public support of an evolving AIDS policy allowed the disease to become a concern more publicly known to the country.

Supporting this call to action was Zachie Achmat, an anti-apartheid and gay activist. Achmat was a co-founder of the Treatment Action Campaign (TAC), established in 1998, when during International Human Rights Day, a group of about fifteen people protested on the steps of St George's Cathedral in Cape Town to demand medical treatment for people living with the virus that causes AIDS, and collected over a thousand signatures calling on the government to develop a treatment plan for all people living with HIV (Robins and Lieres). The location of HIV/AIDS activism within the gay rights movement was central to the formation of TAC due to its foundation in not only public health but human rights in the post-apartheid era. In the dawn of TAC, it was generally assumed that anti-AIDS drugs were beyond the reach of developing countries. Therefore, 90 percent of the world's HIV-positive population was led to a painful and inevitable death. While TAC has mainly acted as a lobbyist to the South African government to provide affordable AIDS treatment, TAC has taken particular action to mobilize the working-class black communities and the trade union movement in South Africa as well.

Progress in treatment, destigmatization, and prevalence of treating HIV/AIDS, however, was actively put at a standstill under President Thabo Mbeki. Mbeki, instead of recognizing the importance of addressing the epidemic, enforced a culture of denialism of HIV/AIDS throughout his tenure, sending letters of doubt to world leaders and inviting scientists to support the claim that HIV did not cause AIDS. However, under relentless pressure from TAC, the July 2002 Constitutional Court made a judgment for the government to make nevirapine, a drug used in the management and treatment of HIV, available to pregnant women infected with HIV, not only in South Africa but universally (MA). This decision was followed by a cabinet statement in October supporting national access to antiretrovirals (ARV). In 2003, the South African Cabinet instructed the health ministry to develop a comprehensive HIV treatment and prevention plan,

and as the government began to disperse HIV treatment at public health care facilities across South Africa, it became more possible to discuss the reality of AIDS without political discourse (Roeder).

Political support swelled after Mbeki's term, and the President of South Africa from 2008-2009, Kgalema Motlanthe, played a significant role in addressing the HIV/AIDS epidemic despite his short tenure in office (Jones and Stokke). Motlanthe emphasized an expansion to antiretroviral treatment (ART), increased funding and distribution efforts for HIV/AIDS programs, worked with international entities to receive aid from global health organizations and donors, and put in the effort to reduce stigma and barriers to care and treatment. Despite Mbeki's denialism and lack of aid, Motlanthe emphasized an evidence-based, proactive approach to addressing the epidemic and laid the groundwork for subsequent administrations to continue expanding upon the field.

TAC, alongside other treatment plans and approaches, has had a significant impact on aiding women. In 2005, HIV infection prevalence in the age group 15-24 years was at 16.9% in women and 4.4% in men (Randall 25). The difference in statistics was highly attributed to factors that were both general and uniquely affected women, such as poverty, violence against women, cultural limitations that promote intergenerational sex, non-condom use, political factors, and challenges that possibly prevented an aggressive response against HIV (Muula). To combat these unique needs, TAC has been at the forefront of efforts in combating HIV/AIDS prevalence among women in South Africa by campaigning to both increase access to care and destigmatize the disease. Specifically, TAC focused on the unique healthcare needs of women regarding sexual health and gynecological care, providing women with education programs and legal care and empowering women through leadership within their own organizations. Reflecting upon HIV response across Africa has also put into perspective the journey of human rights activism, especially for LGBT individuals and women. The importance of governmental support and activism has varied and has either served as a benefit or a long-term consequence for prevailing statistics. Acknowledging the history of activism regarding HIV/AIDS, especially as improvement requires constant innovation, is not only beneficial to aid the epidemic itself but will continue to act as a precedent for furthering women's and LGBT rights to education, autonomy, and power in Africa.

Current Movements and Current Issues with Stigma in African Countries (2019-2023)

Out of the estimated 6000 new HIV/AIDS infections that occur globally each day, two out of three are in sub-Saharan Africa, with young women continuing to bear a disproportionate burden (Kharsany). Women account for 58% of the total number of people living with HIV and have the highest AIDS-related mortality rates (Guenter et al.). In comparison to their male peers, adolescent girls and young women aged 15-24 have up to eight fold higher rates of HIV infections, and the primary mode of HIV transmission continues to be through heterosexual sex (Kharsany). The disproportionately high HIV prevalence throughout the region is a consequence of the lack of appropriate interventions to protect young women and to meet their sexual and

reproductive health needs going into adulthood. Furthermore, marked male-female differences in sexual debut and partners, transactional sex, and sexually transmitted infections (STIs) contribute to adolescent girls and young women's vulnerability to HIV. Pregnancies caused by a lack of reproductive protection have also caused an epidemic in children through vertical transmission.

The COVID-19 pandemic additionally hindered the efforts to aid WLWH in Africa. WLWH disproportionately experiences inequities regarding food insecurity and unstable housing, and therefore, social distancing and safety regulations proved to be either unattainable or unsafe for many women (Closson). A gap in research has formed as the pandemic increased the risk of women, especially in sub-Saharan Africa, as rates of child marriages, teenage pregnancies, educational abandonment, and incidences of sexual and gender-based violence increased, while access to preventive and treatment services for HIV and sexually transmitted infections reduced. The restrictions that COVID guidelines imposed had a significant impact on women who experienced rape or sexual and gender-based violence, significantly as pre-exposure and post-exposure prophylaxis for HIV and other STIs was additionally diminished.

To aid the HIV movement in consideration of a post-pandemic environment, advocate groups and governments have pursued educational and awareness campaigns, increased testing outlets and incentives, integrated technology into a possible solution, and focused on creating support systems to destigmatize HIV/AIDS among WLWH (National Institutes of Health Office of AIDS Research). With the increasing access to antiretroviral therapy (ART), the number of general AIDS-related deaths has steadily declined, along with vertical transmission rates between mother and child, in sub-Saharan Africa, decreasing by 39% between 2005 and 2013 (Guenter et al.). Currently, women from the sub-Saharan African region remain at the highest risk of HIV infection and relevance (UNAIDS). Joint United Nations Programme on HIV and AIDS (UNAIDS) statistics show that the majority of HIV infections occur in this population and region, stating that 3100 of 4000 infections in adolescent girls and young women aged 15–24 years in 2022 occurred in sub-Saharan Africa (UNAIDS). Evidence from previous humanitarian crises demonstrated that adverse maternal consequences were a result of neglect of the provision of essential maternal, sexual, and reproductive health services.

TAC has continued to drive ongoing efforts in HIV/AIDS care, as seen in their partnership with the AIDS Law Project in 2002, where they won a case against the South African government to implement a national Prevention of Mother to Child Transmission (PMTCT) program (Nattrass and Geffen). In 2007, the South African Department of Health (2007) reported that 29.1% of all pregnant women are infected with the virus, and in 2011, the Joint United Nations Programme on HIV/AIDS (UNAIDS) launched the Global Action Plan to reduce new pediatric HIV infections by 90%, by 2015, with the baseline year being 2009 (UNAIDS). The plan, which included India and sub-Saharan Africa as part of the 22 priority countries, alongside other national efforts, has been successful in bringing forward strides in decreasing pediatric human HIV infections, especially in sub-Saharan Africa. In South Africa, new pediatric HIV infections decreased by 84% between 2009 and 2015 (Mnyani).

Community support groups have also been created in hopes that these safe spaces will incentivize women to discuss their experiences, fears, and aspirations without fear of stigma and become more open to care (Mundell). This initiative was inspired by a wide range of research that confirmed positive outcomes associated with psychosocial interventions, such as aiding Patients With HIV Disease that suffered from Depression and Adjustment Disorder (Angelino). These support groups were found to address a wide array of the psychosocial needs of HIV-infected women and facilitate positive change (Health Systems Trust). As feelings of depression, sadness, and isolation are prevalent amongst most individuals with HIV, and even more so amongst WLWH, through identification, modeling, acceptance, and empowerment techniques, patients were able to embark on journeys they described qualitatively as beneficial on several levels (Ncama). Participants reported a personal improvement in mental well-being and lifestyle changes, but also said they became more comfortable talking about HIV in public and with other individuals (Varni et al.). As women are expected to continue responsibilities regarding childcare, housekeeping, and family, their own needs are often seen as a secondary priority (Dossier). Creating a culture of acceptance was beneficial in persuading other women to receive treatment as well, bringing forth the possibility that an HIV-positive diagnosis is no longer the death sentence it was previously perceived to be, and increasing long-term coping skills with women (Gosling).

As the HIV movement evolves for women in Africa, not only have these women been recognized as a priority group for HIV, but they have been involved at the forefront for change. Within the web of complex challenges women face in gender inequality, poverty, cultural factors, and limited access to education of healthcare, women have become increasingly involved in creating initiatives to aid one another. Current organizations and entities, such as TAC, have been mobilizing them to lead, educate, and organize those around them as well (Ahmad). One prominent advocate is Phumzile Mlambo-Ngcuka, who as the former Deputy President of South Africa and Executive Director of UN Women, has been a strong supporter of women's rights in the context of HIV/AIDS and played a central role in the South African government's HIV program, serving as chair of the South African National AIDS Council, taking the lead to ensure broader and more cohesive collaboration with international and civil society partners. As women become involved in political leadership, advocacy, and aid, not only do their contributions aid the HIV movement, but the broader movement of women's rights.

Discussion

This analysis of advocacy movements concerning WLWH in Africa demonstrates improvement over time and the great strides that were made concerning the movement worldwide. This paper focused on how nuanced factors in African history affected how the HIV/AIDS crisis became more extreme and how discrimination and stigma furthered the impact of this particular health issue. HIV/AIDS as a disease has biologically been particularly devestating for women due to the additional implications for mother-to-child

transmission.Between 2015 and 2020, women in Africa had an average of 4.44 children, and therefore were at an increased risk for HIV/AIDS (Galal).

HIV/AIDS rose to prominence during a time of political unrest in Africa, and the dismantling of apartheid rule in South Africa, in particular, was underway. The social and political climate at the time meant that the HIV/AIDS epidemic was a low y priority. However, as a culture of denialism rose and was reinforced under former President Thabo Mbeki, the prevalence of the epidemic grew in some areas of Africa, particularly South Africa. At the same time, the outside world made progress toward remedying the HIV/AIDS crisis. This paper focused on governmental- and externally- led activism and how these organizations mobilized outside partnerships and policy change. At the center of HIV/AIDS activism was the Treatment Action Campaign, and their unique approaches, particularly in South Africa, aided the movement through varied areas, such as leadership diversity, support groups, and education.

Both historical and current advocacy movements worked to destigmatize HIV/AIDS as a disease for women. However, a multifaceted approach is necessary to combat this stigma due to the different barriers that hinder progress toward HIV/AIDS relief for women in Africa. While a typical approach to a public health issue such as HIV/AIDS is usually focused on aiding physical health, a more holistic approach would additionally include mental health support. This would not only include support groups that studies have shown to be beneficial toward destigmatizing HIV/AIDS, but also personal treatment, care, and support. This has been exemplified by the fourth prong of the Prevention of Mother-to-Child Transmission of HIV (PMTCT) approach of the United Nations, which provides care and support, especially during the postpartum stage. Future research should focus on the mental disparities that result from HIV/AIDS, as well as developing culturally, scientifically, and socially relevant approaches to provide care and aid in African regions and globally. Additionally, intersectionality within HIV/AIDS can also be expanded upon, for example, regarding transgender individuals and racial barriers.

This study highlights the gender disparity and political prevalence integrated into the global HIV epidemic. It provides a basis for future studies and interventions on this critical issue for aiding future generations of women. Although advocacy efforts, policy, and scientific disovery has been progressing, there is more work that must be done. HIV/AIDS is not only a public health issue, but must be treated as a social justice issue as well.

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An Overview of Neonicotinoid Environmental Concerns and Impact on Non-Target Species

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Abstract

Neonicotinoids are a class of economically important insecticides, becoming the most-widely used insecticide class in the 21st century. They act mainly as antagonists to nicotinic acetylcholine receptors (nAChRs) through irreversible binding, inducing tetanus and finally, paralysis. In comparison to traditionally used organochlorines, organophosphates, and carbamates, neonicotinoids are a more efficient and cost-friendly choice. However, their direct and indirect threats posed to the surrounding environments of applications and non-target species have come under scrutiny. Presented here is an overview of existing research on neonicotinoid water contamination, impact on soil microbial communities, and degradation patterns, as well as their effects on non-target aquatic species. The linkage of neonicotinoid presence and Colony Collapse Disorder (CCD) in honey bee species is further described, and the pathways of exposure, acute toxicity, and physiological effects on humans is detailed. This paper aims to provide a culmination of existing studies in describing and detailing the concerns associated with increased neonicotinoid usage as their application continues to expand.

Introduction to Insecticides & Neonicotinoids

The exponential increase in the global population over the last century is largely attributed to major advances in the agricultural industry[1]; the decades leading up to and following the green revolution of the 1980s saw the expansion of industrial farming practices, chemical fertilizers, processed foods, and high-yielding variety seeds, increasing crop output and the valuation of the agricultural industry. As of 2023, the global market for agriculture is valued at ~13.3 trillion USD, and that number is projected to grow to ~19 trillion USD by the year 2050. Given the sector's economic

importance as a leading source of revenue generation in many countries, maintaining crop output has been at the forefront of agricultural innovation. Notably, a major task has been to better control insect (e.g. aphids, mites, beetles, thrips, flies, and other bugs) feeding, which is one of the leading causes of crop output loss. Typically, insect feeding coincides with their reproductive cycles and morphological development, and many insects limit stem, stalk, and root growth in plants by continued feeding, thereby reducing the chance of plants surviving to maturity and fruit production. Additionally, grubs and other burrowing insects interfere with mycorrhizae (root-fungi interactions), which reduce the uptake of vital ions and inorganic minerals from the soil. It is estimated that around 30 - 36% of all crops produced around the world are lost to routine feeding by insects[2]. To sustain yields, the usage of chemical insecticides - synthetically produced compounds used to kill target specific insects - has been increasing since the 1940s. Insecticides are divided into two main categories: contact (or foliar) and systemic. Contact insecticides are applied non-specifically on the periderm, waxy cuticle, or other external surfaces of plants, where they can come in direct contact with target insects. In contrast, water-soluble systemic insecticides are applied at specific locations of host plants, where they are uptaken and distributed throughout the plant via vascular tissue. The majority of insecticides used today (including organophosphorus compounds, organochlorines, carbamates, pyrethroids, and diamides) are of the contact type, although many newer classes of insecticides are systemic in nature. The application of both categories depends on the intrinsic chemical properties of the insecticide, the target insects, and regulations on usage.

Approximately 9 million metric tons of insecticides are used annually and their application is expected to continue to increase beyond the year 2050[3]. Further, insecticides represent 60% of all pesticide use, with approximately 6000 individual insecticides in usage[4]. Although traditional insecticides such as organophosphates and carbamates have been extensively important throughout agricultural history and continue to be used in many developing agrarian economies, there has been extensive lobbying for modern alternatives, citing environmental concerns, danger to mammals, and overuse.

Neonicotinoids, or neonics, are synthesized derivatives of nicotine with insecticidal properties. They irreversibly bind to nicotinic acetylcholine receptors (nAChRs) in insect ganglion cells, eventually resulting in full-body paralysis[5]. Neonics are more easily synthesized than many other insecticide classes, and have furthermore been noted to possess an increased target range. These factors have made them a rising force in the global insecticide market, and they now possess a 25% share of the global insecticide market, with over 3000 neonicotinoid products available globally[6,7]. The first commercialized neonicotinoid, imidacloprid, was released in the early 1990s and was heavily used in seed coatings and foliar sprays because of its systemic protection against aphids and mites. Since then, neonics have been an integral part of agricultural pest protection against a host of insects, and have additionally seen menial uses in urban settings as well, present in many insect sprays and poisons. Some

of the highlights of neonicotinoid usage include their relative stability against aquatic and photocatalytic (light) degradation, as well as their ability to travel effectively to all parts of host crops[8]. Although these properties allow for a higher chance of absorption by target insects, they can also lead to environmental accumulation. Residues of neonicotinoids have already been found in food products, surface water, wastewater, and groundwater[9,10]. While neonicotinoids pose less acute toxicity than many other types of insecticides, the environmental and chronic health hazards they pose have not been fully researched, and remains an active area of study[11]. Furthermore, neonicotinoids have been linked to colony collapse disorder (CCD) in the honeybee species *Apis florea* and *Apis mellifera ligustica* (as well as other bee genera)[12]. The connection between neonicotinoids and CCD is discussed further later in this article. Given their extensive uses in agriculture, economic benefits in comparison with other insecticide classes, and environment/health hazards, understanding how neonicotinoids operate and interact with host and target organisms is a necessity. This article will review neonicotinoid development, cellular actions, agricultural uses, and environmental and health hazards.

History & Development

For much of the 19th century, nicotine (in the form of nicotine sulfate) was burned near economic crops to protect against aphids and other bugs. While the effectiveness of this method demonstrated nicotine's insecticidal properties, the chemical was also toxic to mammals, which resulted in the end of its use around 1940. Instead, research shifted to chemically-similar molecules that were less toxic to non-target species in comparison with nicotine. The first precursor to modern-day neonicotinoids, nithiazine, was first synthesized in the 1970s when it was discovered that a class of heterocyclic compounds containing a nitromethylene functional group ($C-NO_2$) could act potently on nAChRs[13]. It was additionally found that this compound was more effective than a variety of then-up-to-date insecticides against the housefly (*Musca domestica*) and other fly species, including the widely-used hexachlorocyclohexane (HCH) and its derivative, lindane. The discovery, which came from Henry Feuer, hinted at the possibility of a wider range of nicotinic derivatives with insecticidal properties. More than a decade later, Schroeder and Flattum confirmed that nithiazine acted as an acetylcholine receptor antagonist that competes with acetylcholine (ACh) for active binding spaces on nAChRs[14]. This was a major breakthrough in insecticidal development, as nithiazine was not an acetylcholinesterase inhibitor (which prevented the breakdown of acetylcholine by acetylcholinesterase) like most insecticides at the time. Following further testing and the addition of an imidazolidine ring $[(CH_2)_2(NH_2)_2(CH_2)]$ to the existing nithiazine structure, the first commercially-ready (and eventually most economically important) neonicotinoid was created: Imidacloprid[15]. The compound was first sold under brand names such as Admire®, Advantage®, and Merit®, although the

number of imidacloprid products available in the market has since grown greatly. Further changes to the base nithiazine structure in the late 1990s led to the release of a variety of neonicotinoid products, infamously thiamethoxam in 1998 and clothianidin in 2001. Imidacloprid, thiamethoxam, and clothianidin were all patented by Bayer AG, a leading figure in the neonicotinoid market that has since patented many more neonic products. Figure 1 depicts the chemical structures of six of the most commonly used neonicotinoids. The first neonicotinoid mixture (developed in 2005) was a foliar spray consisting of various carbamates and the neonic acetamiprid; the spray was widely popular in the United States, where it was used to protect soy and wheat plants from aphids[16]. Since then, neonicotinoids have been heavily utilized for their protection against root-dwelling insects, as well as their specificity against a larger host of insect targets. Additionally, they have been of great economic value to insecticide companies, as neonics are far more profitable in terms of their cost of production-valuation ratio in comparison with organochlorine and organophosphorus-based compounds. Given their popularity, neonicotinoids represent one of the fastest growing sectors of insecticidal research and usage. The development of neonicotinoids from the base nicotine/nithiazine molecules to the current selection of neonics is notably also a reflection of scientific advances; the use of X-ray crystallography patterns, mass spectrometry, and inorganic chemical synthesis, as well as new understanding of neural receptors and their interactions have played a crucial part in advancing neonicotinoids through the past few decades.
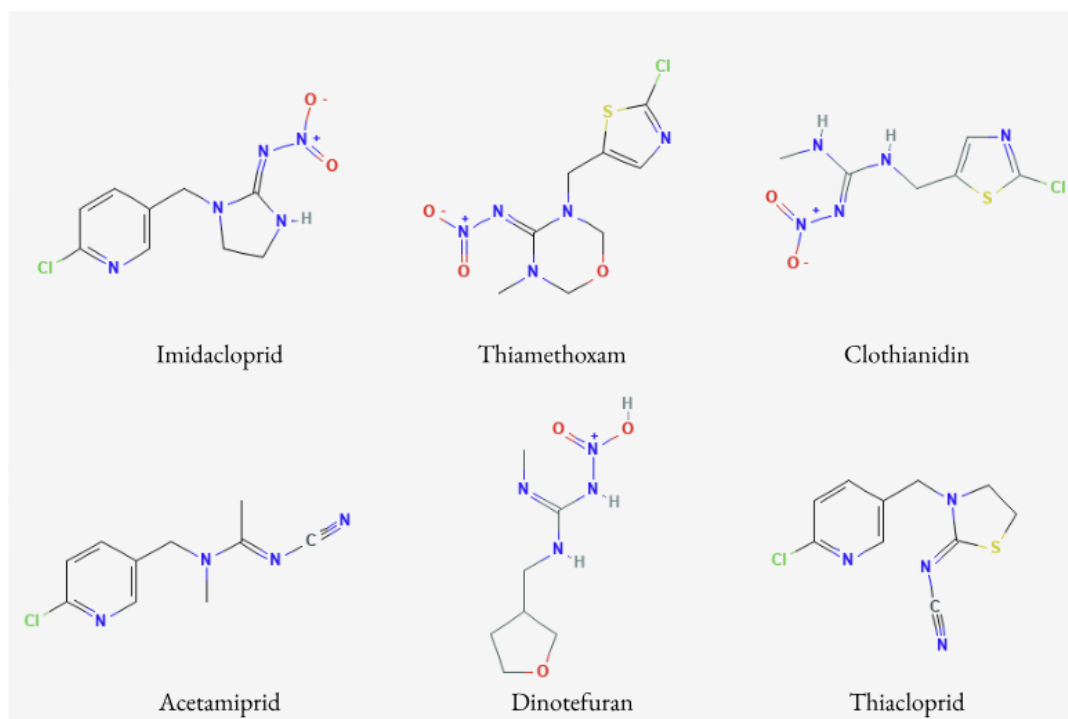

Figure 1: Chemical structures of the six most commonly used insecticides globally.

Structure & Mode of Action

Neonicotinoids, which have similar chemical properties to the chemical nicotine, are aromatic heterocyclic compounds that can be divided into two main groups: N-cyano amidines and nitroguanidines. The prior consists of a R-C≡N cyanoamidine functional group attached to a nitrogen atom on the central neonicotinoid structure[17]. Examples of N-cyano amidines include the neonics acetamiprid and thiacloprid. Nitroguanidines, on the other hand, are neonics with a nitro ($R-NO_2$) functional group bonded to a central nitrogen atom. Imidacloprid, thiamethoxam, and clothianidin are all examples of nitroguanidine neonics. Nitroguanidine compounds are less reactive with mammalian and non-target receptors, which is why they are more common in agricultural settings[18]. A key feature of neonics is the presence of an elastic bond between the defining functional group and the base heterocyclic structure. All neonics are water-soluble and electronegative in charge, which allows them to be taken up by the root via ion-gated channels selectively permeable to hydrophilic substances. Neonics are then transposed to all vascular and nonvascular segments of the plant - from the fruit to the leaf. Thus, a major advantage of systemic neonicotinoids is their ability to protect the whole plant, unlike contact insecticides, which rely on direct interactions with insects. The insecticides themselves pose little damage to the host crops, however, the effects that neonicotinoids have on ion balances within plant cells is an ongoing area of research[19].

Once ingested by target insect species, neonicotinoids work to disrupt neural activities by targeting receptors at postsynaptic junctions on neural pathways. Specifically, these insecticides interfere with the activity of the nicotinic acetylcholine receptor (nAChR). *Reversible* binding of neurotransmitter acetylcholine (ACh) to a nAChR causes swift depolarization of the cell membrane, thereby communicating a neural signal[20]. To reestablish ionic balance and repolarize the membrane, acetylcholine is hydrolyzed into acetic acid and choline by the enzyme acetylcholinesterase (AChE). Following a neonicotinoid binding to a nAChR, a typical action potential is registered and appropriate cell mechanisms take place. However, neonics bind *irreversibly* to nAChRs, meaning that AChE is unable to perform hydrolysis and action potentials are sustained throughout the refractory period[21]. On a larger scale, this leads to tetanus and, eventually, full-body paralysis of the target insect. Figure 2 describes the binding of neonicotinoids to nAChRs in comparison with the biomolecule ACh. Thus, neonics are competitive inhibitors that disrupt homeostatic behavior in neural and neuromuscular regions.
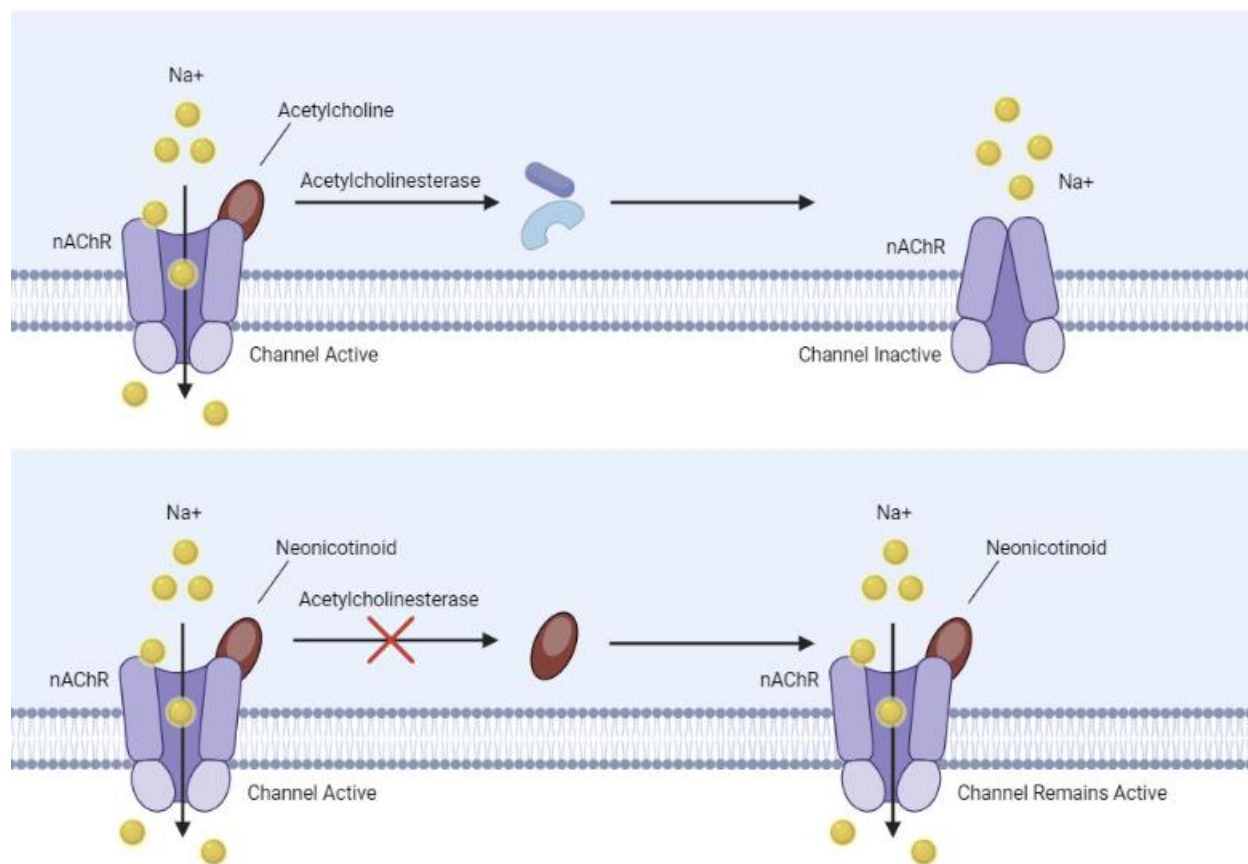
Figure 2: Reversible binding of acetylcholine to an acetylcholine receptor (top) in comparison with irreversible binding of a neonicotinoid (bottom).

Neonicotinoids are effective against most insects because the insect brain possesses a high density of nAChRs, increasing the probability of successful binding to a receptor. Insect nAChRs are made up of three α-subunits (loops A-C) and three non-α-subunits (loops D-F) that make up the allosteric binding site for ACh and neonics[22]. While it is still being studied, a potential reason for neonicotinoids' heightened target specificity in comparison to older insecticide classes is the varying spatial configurations of nAChRs between insects and non-target species classes. In mammals, there are many types of nAChRs with varying loop counts and thus varying structures, so the likelihood of neonic binding is low[23]. Specifically, neonicotinoids have been proven to be most effective against the α4β2 receptor (made up of α4 and β2 subunits), which comprises almost all of insects' nAChRs, but only ~10% of human and other mammalian nAChRs. The other ~90% is made up of other nAChR variations to which neonicotinoids have low to moderate substrate binding properties[24]. Homomeric (singular type of subunit) examples of such other nAChRs in mammals include the α7 and α9 receptors, while heteromeric (two or more unique subunits present) examples include the α3β4 and αβε(γ)δ receptors. Regardless of this variation, mild toxicity has been noted in non-target species; the

effects of neonics on humans are discussed in detail later in this article. In addition, neonicotinoids in partially or fully degraded forms can interact with enzymatic reactions in a wider variety of species, including microbial communities, thus expanding the potential range of species affected (though effects are depressed).

The precise dosage of neonicotinoids is critical and is influenced by a variety of factors including the type of neonic used, the insect species, the target insect's morphological stage, and the arrangement of the protein nAChRs in the central nervous system. As such, the dose requirements of the same neonicotinoid might vary based on the target insect. Furthermore, the general toxicity of related neonicotinoid insecticides in comparison with one another must be considered. To compare the relative acute toxicity of related neonics (or any class of insecticides), it is standard practice to use a model insect, such as the housefly (*Musca domestica*) or the Japanese beetle (*Popillia japonica*). Table 1 depicts the dosage of varying neonics required to kill 50% [LD_{50}] of the common true bug *Apolygus lucorum*, as per a study by Pan & Lu [2014][25]. There are various guidelines regarding neonicotinoid applications from prominent sources of authority such as the EPA, EU, and the Australian PVMA. Slight deviations in recommended application quantities likely stem from different tolerances of runoff and neonic presence in water/food sources.

Table 1: LD_{50} ranges for different neonicotinoids on *Apolygus lucorum* (adapted from Pan & Lu).

Neonicotinoid	Median LD_{50} (ng/adult *P. japonica*)
Imidacloprid	8.94
Nitenpyram	5.68
Acetamiprid	8.69
Thiamethoxam	17.39
Dinotefuran	10.79
Thiacloprid	12.32
Clothianidin	14.95

Environmental Risks of Neonicotinoids

While neonicotinoids present economic advantages compared to other organic and inorganic insecticides classes, they come with a set of defined concerns. Specifically, their effect on non-target species (including microbial communities) is a point of note. There has been considerable research into the negative physiological effects [sublethal or lethal] on different species with acute or prolonged exposure to neonicotinoids. As so, a discussion of neonic effects on surface water - home to many affected aquatic species - is presented. Additionally, the dangers posed by neonicotinoid contamination of aquifers and soil is stated, while a brief mention is made on the bioaccumulation and degradation patterns of the insecticides. Given the continued usage of neonicotinoids under the assumption of being a 'safer' alternative to organophosphorus compounds, organochlorines, carbamates, and other insecticide classes, a discussion on the comprehensive risk of using neonics on the ecosystem is necessary.

Surface Water Contamination

A major environmental concern of neonicotinoid application is the threat it poses to surface water; the presence and effect of this insecticide in freshwater sources near agricultural settings is an area of active research. Neonicotinoids can enter surface water through various routes, although primary accumulation has been noted through surface runoff in the water[10]. A study by Berens et al. [2021] found that only 1% of neonicotinoids applied through foliar sprays and 3% of neonicotinoids applied in seat coating are actively uptaken during ion exchange. The limited sorption of neonicotinoids is modeled through a linear isotherm, with varying sorption coefficients, K_C. The observed sorption coefficients of thiamethoxam, imidacloprid, and clothianidin were ordered in K_C (Thi. > Imid. ≈ Clot.) In various observed tests, K_C of neonicotinoids ranged from 1.5 - 5 gL^{-1} (p < 0.05), indicating slow, positive uptake of neonicotinoids into plant taproot[26]. It should be noted that many of the related studies in this area were performed in controlled settings, which differ greatly from environmental conditions found in nature. Specifically, precipitation and resulting surface runoff are examples of dynamic properties of water [and dissolved solutes] movement. Neonicotinoids, when applied in the soil, tend to accumulate in specific hydrophilic regions from where they are uptaken through ion exchange. Such regions are typically found in topsoil - a layer susceptible to movement of solutes and water[27]. Thus, precipitation and excessive water concentrations can lead to surface runoff, where these neonicotinoids are transported to larger water sources, including lakes, rivers, streams, backwaters, marshes, and ponds.

Further, neonics can also enter surface water through other forms. In urban settings, dissolved neonicotinoids can pass into freshwater through wastewater treatment plants (WWTPs) water

expulsion[28]. This is more common in developing nations with limited filtration infrastructure. Neonic presence in watersheds additionally factor into their ability to travel from smaller, contained bodies of water to larger, uncontained regions. Leaching from groundwater sources into surface water through simple diffusion is furthermore observed in certain hyporheic zones, where chemical exchange occurs with the surrounding surfaces. Neonicotinoids can also enter the atmosphere through the process of adsorption, where they attach to larger pollutant molecules, mainly frass, the solid excreta of insects and other species[29]. Here, concentration gradient-driven gas exchange at the air-water interface facilitates the diffusion of neonicotinoids into the water source. While these different actions impact the ability for neonicotinoids to enter surface water, <40 ng - 100 μgL^{-1} have been noted in certain trials, indicating both the limited effect on neonic presence as a dissolved solute in comparison to surface runoff and direct accumulation, where over 500 μgL^{-1} have been noted in samples.

Neonicotinoids in a dissolved state have lower toxicity towards aquatic life in comparison with foliar and systematic applications on economic crops[30]. However, acute toxicity of imidacloprid, thiamethoxam, and clothianidin, amongst other neonic derivatives, have been observed on both vertebrate and invertebrate species. In the former, the insecticides act directly upon nAChRs in the central nervous system while in the latter, they act upon analog receptors in circular nerve nets or organized ganglia. Spectrophotometric assays performed by Butcherine et al. [2021] found sublethal effects on the juvenile Black Tiger Shrimp (*Penaeus monodon*) that included reduced enzymatic activity of acetylcholinesterase, catalase, and glutathione S-transferase in abdominal tissue[31]. Additionally, limited spasmodic movement was noted in neonicotinoid-exposed experimental units in this and other studies when compared to controls, which corresponds to the over-propagation of action potentials in select muscle cells when exposed to neonicotinoids. Acute toxicity (LD_{50} following ~2 days) was determined as 1 μgL^{-1} in clothianidin, <400 μgL^{-1} in thiamethoxam, and >408 μgL^{-1} in imidacloprid. A long-term static renewal study on the effect of neonics on the freshwater invertebrate *Hyalella azteca* further found that mobility was affected at insecticidal concentrations nearly 60 times lower than the LD_{50}[32]. Reduced survival rates were also noted acutely in post-larval shrimp following exposure to imidacloprid and a close analog, fipronil when placed in environmentally challenging conditions. Indicated here are the major sublethal effects of neonicotinoids in non-target species, as well as the complex effect of bioaccumulation in aquatic species. The cherry shrimp *Neocaridina denticulata* had reduced locomotive activity and gill ventilation, similarly to the effect on other shrimp species of the same genus[33]. In the small freshwater Chinese minnow (*Rhynchocypris oxycephalus*), when neonicotinoids were present in 0.1 - 2.5 ppm, oxidative stress increased, while the production of immunoglobulin M was downregulated by reduced signaling transmission[34]. The complex effects described as a result were reduced immune functioning and protection against pathogens. While these and other similar studies indicate definable sublethal (and in some cases, lethal) effects of dissolved neonicotinoids at LD_{50} or similar concentrations, the typical concentration of dissolved

neonicotinoids in surface water samples is far lower than that of the selected experiments[35]. However, the results of various studies suggest that even when found in trace quantities (defined here as <5 ppm), there are observable effects on aquatic creatures, and even if not lethal or sublethal, speaks to the importance of limiting the entry of neonicotinoids into surface water.

Effect on Groundwater

Similar to surface water, groundwater (stored in porous aquifers) is prone to neonicotinoid leaching; such contamination carries serious public safety hazards given the dependence on groundwater as a source of drinking water in many parts of Asia, Africa, and South America[36]. The general structure of a groundwater system consists of a discharge (surface-air interface), unconfined aquifer, confining bed, and a confined aquifer. Most drilling activities rely on the presence of drinking water in the confined aquifer region. It was previously assumed that the water in this region was pure, and thus, an informal filtration process was often the standard in areas dependent on groundwater[37]. However, weak rock-soil interfaces in agricultural settings allow for the leaching of water (and its dissolved contents) from the surface to the unconfined and the confined aquifer. Of the dissolved substances, neonicotinoids have been identified in many studies to be present in confined aquifers in an active, partially active, partially degraded, or fully degraded state, as measured by mass spectrophotometry and ion-exchange chromatography. Figure 3 provides an overview of the process of insecticide contamination of groundwater.
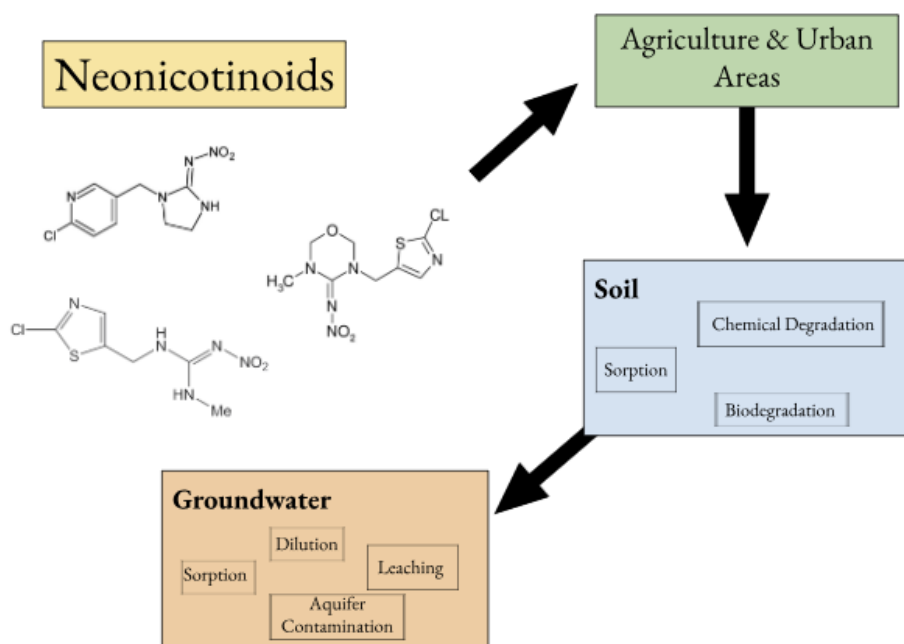
Figure 3: The process of transformation and contamination of neonicotinoids in groundwater aquifers.

Monitoring of hyporheic zones in riverbeds for the presence of neonicotinoids in an Iowa economic soy crop region found that the insecticides were present at 0.13 - 0.98 ppm. The rate of simple diffusion into unconfined aquifers occurred at ~14.4% per hour, which is partially due to the pressure exerted from the surface water above[38]. The Thompson et al. [2021] article found that rates of neonicotinoid absorption were directly proportional to both the quantity of neonicotinoids applied and the porous structure of the aquifers. A study on the prevalence of neonicotinoids [and sulfoxaflor] in alluvial (clay, silt, sand, etc.) aquifers identified the presence of imidacloprid, thiamethoxam, clothianidin, acetamiprid, dinotefuran, and thiacloprid. While only trace quantities of acetamiprid, dinotefuran, and thiacloprid were found, 73% of the studied aquifers contained statistically significant quantities of either imidacloprid, thiamethoxam, or clothianidin. It has been established that clothianidin is most susceptible to groundwater leaching, although the reasons for the increased rate of gradient-based diffusion remains unknown[39]. Quantitative ranges of different neonicotinoids' presence in confined aquifers have been established from various studies: 34 - 391.7 ngL^{-1} (clothianidin), 6.7 - 42.4 ngL^{-1} (imidacloprid), and 0.2 - 1.6 ngL^{-1} (thiamethoxam).

A pilot study in midwestern United States - where neonicotinoids reign as the most popular insecticide - found that from 47 assessed groundwater samples, neonicotinoids were present in greater than 50%, with two or more present in greater than 10%. Clothianidin was the most frequently detected in the analyzed well water, present in 55% of all samples with a maximum concentration of 140.5 ngL^{-1}. Imidacloprid and thiamethoxam were found at 13% and 6% of all samples, with maximum concentrations of 29.3 ngL^{-1} and 13.1 ngL^{-1}, respectively. In addition, the effects of contaminated groundwater contamination were demonstrated through chemical separation analysis of urine[40]; Human exposure could be seen in the presence of ~10 neonicotinoids or transformation products in urine samples; Clothianidin, imidacloprid, and thiamethoxam were found at ~4.7 μgL^{-1}, 1.4 - 1.6 μgL^{-1}, and 3.2 - 3.4 μgL^{-1}, respectively. Most of the partially degraded transformation products were detected in trace quantities, although the presence of acetamiprid-N-desmethyl at 16.9 μgL^{-1} in urine samples indicates either a potential degradation metabolic pathway or a degradation process prior to consumption[41]. The results of the pilot experiment represent the quantitative presence of functional neonicotinoids in groundwater (unconfined and confined), as well as their persistence following passing through the human metabolic system. This necessitates a serious consideration of groundwater filtration processes and their effectiveness in limiting the passage of neonicotinoids into drinking water. Additional research is required into the process by which neonics pass through from the surface into confined aquifers, in addition to the partial degradation patterns that occur when present in aquifers.

Impact on Soil Microbial Communities

Neonics can remain in the soil for a prolonged time, as the systematic uptake through direct interactions with roots or via hyphae (fungal network) is a slow process[42]. While present in the soil, the insecticides are subject to leaching, biodegradation, and chemical transformation. Different chemical natures of varying soils (e.g. pH, temperature, density, water content, etc.) additionally influence the fate of the neonic.

Topsoil is generally a ground for rich microbial growth and diversity, given the abundance of organic matter as energy. However, it has been indicated that the presence of neonicotinoids in soil (in either a functional or semi-functional state) can possess acute adverse effects on the homeostasis regulation of microbes.

Neonicotinoid, cyclic urea, cyclic guanidine, nitroso, and other insecticide derivatives are degraded by certain eukaryotic and prokaryotic microbes; eukaryotic genera *Apiotrichum*, *Gamsia*, *Humicola*, *Kitasatospora*, *Solicoccozyma* and prokaryotic genera *Sphingomonas*, *Streptomyces* and *Terrabacter* possess catabolic pathways involved in the metabolism of heterocyclic, aromatic compounds such as neonicotinoids[43]. Specific biodegradation patterns are discussed in the following sections. In a controlled environmental setting, it was found that close to 45% of identifiable microbial communities experienced negative change in population growth in the presence of different neonicotinoids[44]. Labrie et al. [2020] further concluded that anywhere from 0 - 42% of Hay bacillus (*Bacillus subtilis*) showed reduced rates of cell division, protein output, and growth following exposure to thiamethoxam imidacloprid, and clothianidin ($p < \sim 0.3$)[45]; negative homeostatic changes observed were minimal, yet remained statistically significant. Soil microbial population change of *Ensifer adhaerens* was determined by assessing select spectrophotometer samples, revealing a negative change in the population size index of selected microbial populations[46]; quantitative analyses of diversity changes were limited due to the presence of external, uncontrolled chemical factors, including changes in pH and temperature. Both of the presented studies confirm a correlation between increased neonicotinoid presence and negative homeostatic changes, although direct causation was not established in either test. In the ammonia-oxidizing archaea community *Methylotenera* and some nitrifying/nitrogen-fixing communities, the ability for organisms to successfully engage in nitrogen-cyclic metabolic pathways was limited when imidacloprid was applied at high concentrations[47]. The change in populations of these microbial communities ranged from 3 - 6.3%, and it is plausible that negative neonicotinoid interactions with the nitro-reducing enzyme nitroreductase was responsible for the inability for certain microbes to efficiently convert atmospheric $N_2 \rightarrow NH_3$. While these and other conformational studies indicate the toxicological effects of neonicotinoids on species without nervous systems or nerve nets, there have been many experiments which note no change in population size, density, or overall functioning of certain microbes when

exposed to neonicotinoids[48]. Thus, the effect of insecticidal exposure on select soil microbes is directly correlated to the soil conditions, species-specific toxicity variations, and degradation patterns of the neonics in both intracellular and extracellular settings.

There has been limited research regarding the specific interactions occurring between neonics and microbial enzymes that result in changes in cell functioning. However, certain pathways impacted by the presence of partial binding of select neonicotinoids have been noted through the use of X-ray crystallography and protein separation analysis. Dimeric avidins, biotic-binding proteins part of the microbial defense system against extracellular disease vectors, were underexpressed when neonicotinoids thiamethoxam and acetamiprid were present[49]; an unusually high presence of avidin in the form of an avidin-vitamin complex indicates reduced cell viability and/or proliferation. Additionally, it is presumed that the reduced production of dimeric avidins acts secondarily in limiting microbial populations by reducing protection against other harmful species and viruses. The enzyme responsible for oxidizing reduced pyridine nucleotides (NAD, NADP), hydroxyacid oxidoreductase, was found to be – unlike dimeric avidins - overexpressed in *Rhizobium* microorganisms in the presence of significant quantities of neonicotinoids (specifically, a heterocyclic derivative of imidacloprid)[50]. It is proposed that the balance between oxidized and reduced NAD and NADH in the cell is affected by the overexpression of hydroxyacid oxidoreductase, altering the ability for cells to undergo the citric acid cycle and oxidative phosphorylation efficiently. Additional studies are required to validate this hypothesis. Other studies have found that neonics and partially degraded derivatives can act as cationic aromatic substances (similar to the nucleotides themselves) capable of hydrogen bonding with the base reservoir of the DNA helix[51]. Through groove binding, thiacloprid and imidacloprid were observed to insert themselves through weak interactions in the DNA ladder itself. The resulting destabilization of the macromolecule results in a slight increase in the length of the DNA molecule and a slight decrease in thermal stability. While the understanding of the effects of such interactions are still limited, interactions with any functional macromolecule - specifically DNA, RNA, and proteins - can have strong implications for gene expression.

In addition, certain physiological processes have been identified to be either upregulated or downregulated by the intracellular presence of neonicotinoids although knowledge of the enzymes and substructures specifically affected have been limited. Biodegradation processes are made up of various enzymatic pathways, and it has been shown that prolonged, extensive exposure to certain neonicotinoids in soil microbes result in reduced *N*-deacetylation and oxidative cleavage[52]; the prior plays a key role in the folding process and stability of proteins, while the latter introduces different functionalities to complex molecules. One study concluded a weak correlation between the quantity of neonicotinoid and the level of suppressive methylations pertaining to certain deacetylation proteins in the roundworm species[53]. However, the overall understanding of the effect of neonics in soil

microbial communities remains limited, and a greater depth of research is required to understand the effects of their presence in prokaryotic and eukaryotic microbes' homeostasis.

Degradation Patterns

In the environment, neonicotinoids are prone to degradation into smaller, organic or inorganic compounds. Metabolites resulting from degradation may be rendered ineffective in acting against insects, while some may still maintain insecticidal properties[54]. This subsection discusses the different processes by which neonics are degraded in the environment following their application and associated concerns.

Microorganisms of the genera *Apiotrichum*, *Gamsia*, *Humicola*, *Kitasatospora*, *Solicoccozyma* *Sphingomonas*, *Streptomyces* and *Terrabacter* possess specific catabolic pathways for neonicotinoid degradation through enzyme-substrate catalysis. Acetamiprid breakdown analysis using chemical separation techniques (relying on known degradation patterns) found that nitrile hydratase was acted upon in *Ensifer meliloti* and *Streptomyces canus*[55]. Specifically, a transformation pattern of acetamiprid into the metabolites IM-1-2, IM-1-4, and IC-0 was noted in a linear degradation process. Additionally, a protein coded for by the *ahnA* gene in *E. meliloti* responsible for the transformation of acetamiprid to IM-2-1 was identified as being a factor in neonicotinoid degradation. The N-desmethyl metabolites IM-1-2 and IM-2-1 have been identified to possess limited acute toxicity to soil microbes and roundworm species, suggesting that microbial degradation may further reinforce negative effects of neonicotinoids in the environment.

Thus far, around 29 genes and 10 proteins have been identified in the partial or full degradation of imidacloprid in various microbes. CYP353D1v2, a cytochrome p450 enzyme/coenzyme, has been identified as a primary enzyme responsible for microbial biotransformation of neonicotinoids[56]. A substrate depletion test identified that when overexpressed, the cytochrome is responsible for the creation of an unknown heterocyclic compound that showed insecticidal properties corresponding to minor sublethal changes in behavior. Microbial degradation of neonicotinoids, seen through the insecticidal properties of degraded products, does not serve any purpose; rather, the insecticides possess similar structures to beneficial or useful heterocyclic compounds. YK-624, a catalyst-enzyme present in certain *Stenotrophomonas* microbes, has been shown to cleave a nitroguanidine functional group from the structure of clothianidin, resulting in the formation of methyl nitroguanidine and 2-chloro-5-methyl thiazole[57]. Both of these compounds were further degraded into either cationic or uncharged aliphatic substances. Of the degradation patterns observed through YK-624, certain products were eventually oxidized to carbon dioxide, while others possessed a limited association with a decrease in *Stenotrophomonas* populations (relationship needs further clarification). Other patterns identified include removal of amidine groups from imidacloprid,

thiamethoxam, clothianidin, and acetamiprid through the use of deaminase and N-deacetylase, resulting in varying metabolites with similar, less, or no insecticidal properties in comparison to the reactant insecticide, respectively.

While there is much to learn on the methods by which soil microbes can degrade anywhere up to 60% of neonicotinoids applied, a focus must be directed towards the impacts of the metabolites on other soil microbes, non-target organisms, and their presence in surface water and groundwater. There have been certain correlations drawn to a negative environmental effect, but additional studies are required to identify the enzymatic causes of the observed relationships.

Another form of neonicotinoid degradation is through photocatalytic means, which uses light energy to drive advanced oxidative catabolism. Specifically, absorption of photons at specific wavelengths causes electron excitation and oxidation of larger molecules, creating cleaved products. The excitation of electrons in neonicotinoids mainly occurs in hydroxyl radicals (-OH), and can result in the formation of weak acids, such as 6-chloronicotinic acid[58]. Degradation caused by the formation of carbonate and oxygen-based products is referred to as indirect photolysis, while degradation from sunlight is direct photolysis[59]. Neonicotinoids, like many other insecticides, are prone to breakdown from both direct and indirect photolysis. In experiments using photodegradation lamps, it was found that anywhere from 8-25% of the neonicotinoids present in a soiled surface were partially degraded over the course of 48 hours, with thiamethoxam being most susceptible to degradation, followed by clothianidin and imidacloprid[60]. In water, the half-life of neonicotinoids varies greatly, and typically depends on the pH, temperature, and molarity[61]. Direct photolysis has resulted in the degradation at a half-life range of 12 min (imidacloprid) - 42 hours (thiamethoxam), while indirect photolysis of imidacloprid results in a half-life range of 5 hours - 19 hours[62]. The varying half-life values depend on the quantity of photoenergy supplied. At a 270 nm light wavelength (indirect photolysis), thiamethoxam and imidacloprid were nearly 87% degraded, with other derivatives following at ~75 - 83%, indicating susceptibility of certain chemical components in their respective structures to excitation. However, there have been limited studies that emulate realistic environmental conditions, where the balance of direct and indirect photolysis is in constant flux[63]. Additionally, there has been little research on how the chemical products of photolysis affect aquatic and terrestrial life, although some studies describe the effect of agriculture on photolysis in surface water; many water bodies near agricultural settings are more sediment-impaired, meaning more light scattering (direct photolysis impaired), and thereby a longer degradation half-life[62]. This has been a factor in explaining the extensive presence of neonicotinoids in large water sources for long periods of time.

A major process by which neonicotinoids are degraded in the environment is hydrolysis in bulk water. In large samples of water, such as in lakes, rivers, and estuaries, neonicotinoids interact with different solutes and dissociated products; in a theoretical study involving dinotefuran found that at a C-1=N-2 bond, a proton transfer to N-2 (from interactions with hydroxyl) creates an unstable

product, prone to degradation[64]. Similarly, in alkaline water conditions, thiamethoxam was observed to react with minerals and water itself to form more stable guanidine compounds, such as aminoguanidine (or pimagedine)[65]. Concerningly, pimagedine (and certain other products from neonicotinoid hydrolysis) has antimicrobial and acute insecticidal properties[66].

Hydrolysis of imidacloprid at a certain energy level can form 8-Hydroxydeoxyguanosine (8-OHdG), an oxidative reactant known to be a marker of DNA damage[67]. Certain second-level hydrolysis reactions may form more toxic - even carcinogenic - products, such as the formation of hydroxylamine and protonated nitrogen ions from a degraded thiamethoxam. Hydroxylamine has been linked to certain forms of bladder cancer if present in heightened levels in human urine[68]. Additional research is required to better understand the environmental risks posed to agricultural communities by neonic hydrolysis, as most studies regarding the matter are performed in controlled settings.

Neonicotinoids have also been noted to be subject to partial or complete degradation (into simpler heterocyclic or inorganic compounds) through exposure to hard metals, volatilization, or other abiotic transformations[69,70]. As far as biotic transformations go, it has become of increasing concern the effect of neonicotinoids in their degraded states on non-target insects and mammals, including a potential toxicity to humans. Studies on the degradation patterns *in vivo* have shown mild to severe effects on non-target species, encompassing sublethal and lethal effects, depending on the species[71].

Linkage to Colony Collapse Disorder

Honeybee colonies play a crucial role in shaping ecosystems by acting as pollen distributors. Bees contribute over $30 billion USD to the global agricultural market and collectively make up one of the most economically important sets of insect species. Colonies are composed mainly of worker bees, drones, and a queen, and remain active typically throughout the winter season and while food supply is present; they are only abandoned if structural damage is present or the queen bee dies. Colony Collapse Disorder (CCD) is an abnormal phenomenon in honeybee species where worker and drone bees disappear, leaving their colonies, queen, and young alone[72]. Many beekeepers reported abnormal behaviors in bees arising from CCD-affected colonies, including reduced foraging ability, bees not returning to the colony, and disorientation[73]. The disorder was first described in Europe, 1998, where upward of 50% of certain western honeybee *Apis mellifera* colonies saw a sharp decrease in the number of male workers and drones in the wild[12]. In the United States, the winter seasons of 2006-2007 and 2007-2008 saw large-scale withdrawals of managed *A. mellifera* populations, resulting in upward of $1 billion dollars in losses. A study of over 400,000 American managed colonies conducted

in 2008 found that 35.8% of all colonies reported partial or total losses of worker bees; of these colonies, nearly 60% did not identify dead bees present, a primary symptom of CCD[74]. There have been various theories identifying the main causes of CCD, including the ectoparasitic mite *Varroa destructor*, various endoparasites, airborne viruses (such as the chronic bee paralysis virus), and notably, chemical insecticides[75]. As such, studies have shown that the use of neonicotinoids, especially imidacloprid, have detrimental, sublethal effects on different pollinator bees which have been in turn linked to CCD.

Neonicotinoids are permitted to be applied at different times of the year depending on the crop in question, and are translocated to the pollen and nectar of the affected plants, explained by their systemic nature[76]. Thus, there is a direct potential for honey bees in proximity to agricultural settings to be exposed to neonicotinoids at various sites, as well as for the insecticide to be present in the nectar they collect. It should be noted, however, that given the reduced quantity at which neonicotinoids are applied compared to older insecticides, the exposure to bees is prolonged, rather than acute. Established pathways discussed here include majorly exposure through food, as well as interactions with contaminated plants, water, and spray drift (direct exposure). There is, however, significant variability in existing data regarding neonicotinoid exposure to bees, in part due to the large foraging range, variation in different colonies, and difficulty in identifying a singular cause to CCD[77]. Different honey bees with different roles in colonies are exposed to neonicotinoids in different ways; for instance, worker bees do not consume pollen or pollen grains, but instead bring it back to their colonies where other types of bees, such as nurse bees and immature young, do consume them[78]. Such variability further makes it difficult to triangulate a primary source of neonicotinoids in colonies suffering from CCD.

A study conducted in Europe (2006) found that nearly 70% of pollen collected from 125 samples contained either significant or trace quantities of imidacloprid, 6-chloronicotinic acid, and 35 other derivatives[79]. Here, imidacloprid was found at quantities ranging from 1.1 - 5.7 μgKg^{-1}, 6-chloronicotinic acid at 0.6 - 9.3 μgKg^{-1}, and a close derivative, fipronil, was found in 9 samples at elevated levels (>10μgKg^{-1}). Another 3-year study identified the presence of imidacloprid and clothianidin in various plant nectars [~41% of tested samples] at concentration ranges of 0.3 - 5.4 micrograms per kilogram[80]. That same study found elevated levels of thiamethoxam on guttation drops of oilseed rape plants. Honeybees of *A. mellifera* were noted to interact with these guttation drops and trace quantities of applied thiamethoxam were found in various tested colonies. Imidacloprid and dinotefuran residues were furthermore found in over 98% pollen coating of tested pumpkin plant in a 2012 study; the study identified parent neonics from various detected metabolites, including desnitro olefin, urea, and 6-chloronicotinic acid[81]. In the common cantaloupe *Cucumis melo var. cantalupensis*, up to 4 mgL^{-1} of imidacloprid was recorded on dew particles, with additional findings on the presence of imidacloprid and cyclic urea in beeswax produced by the same bees that

interacted with the dew[82]. The study completed by Girolami et al. [2009] not only identified a linkage to CCD in >50% of tested colonies, but furthermore noted that various drone and worker bees sampled died within minutes of exposure, indicating a lethal effect posed by exposure to the insecticide. In addition, Zhang et al. [2023] found that the increased bioavailability of imidacloprid in controlled soil settings corresponded with decreased foraging and desire for food - trademark signs for CCD[83].

A leading critique of the idea that neonicotinoids have a direct impact on CCD has been that honey bees can identify sources with neonic coating present, be it in nectar, pollen, or guttation drops. However, it was discovered in 2015 that both *A. mellifera* and *Bombus terrestris* bees do not avoid nectar-relevant concentrations of imidacloprid, thiamethoxam, or clothianidin[84]. Rather, bees preferred sucrose solutions with both imidacloprid and thiamethoxam present over regular sucrose solutions. Neonicotinoids stimulations did not excite any sensory or sucrose-sensitive neurons at statistically significant levels compared to trials, indicating an inability in bees to recognize neonicotinoids in undegraded forms. Thus, neonics pose a major environmental risk by acting as a physiological detriment to bees while maintaining no sensory deviation from normal food. Nectar containing neonicotinoids is unknowingly passed to nurse bees and larvae as a result, where consumption of the toxic insecticides occurs. The presence of neonicotinoids [in concentrations greater than $5\mu gKg^{-1}$] in pollen collected by drones has shown to create a significant decrease in nurse bee populations, along with reduced carbohydrate and lipid metabolism in larvae[85].

Neonicotinoids possess extreme acute toxicity to most bee species, with an LD_{50} in the ranges of nanograms per individual. Studies identify the orchard mason bee *Osmia lignaria* as the most susceptible to lethal and sublethal detriments from continued exposure to neonics (specifically clothianidin), followed by *A. mellifera*, *B. terrestris*, *Megachile rotundata*, and other members of the *Apis* and *Bombus* genera, in that order[86]. Dust scattering, in particular, has been proposed as a second major source of neonicotinoid ingestion, in addition to consumption of food. Despite the advent of improved seed coating techniques, expulsion of neonicotinoid particles into the air are prone to occur in large quantities due to agrotech limitations. Neonicotinoids typically remain airborne after being adsorbed by larger gaseous particles, including water vapor. An increase in humidity has been established to have a positive correlation on the quantity of insecticide absorbed, as has increased sunlight and temperature, although the reasons for this phenomenon are currently under active research[87]. Airborne particles are not only a threat due to their physiological impact on active worker bees, but also to the hive, in both indirect and direct fashion; if in close proximity to an application of neonicotinoids, a colony is susceptible to direct airflow containing contaminants, and there is a constant issue of the contaminant being brought back with worker bees. Advancements in agrotech limiting the air scattering of applied insecticides would cut down on the environmental risks posed to

bees through airborne inhalation. Figure 4 depicts a summary of the different sources of neonicotinoid exposure for bees as it relates to CCD.
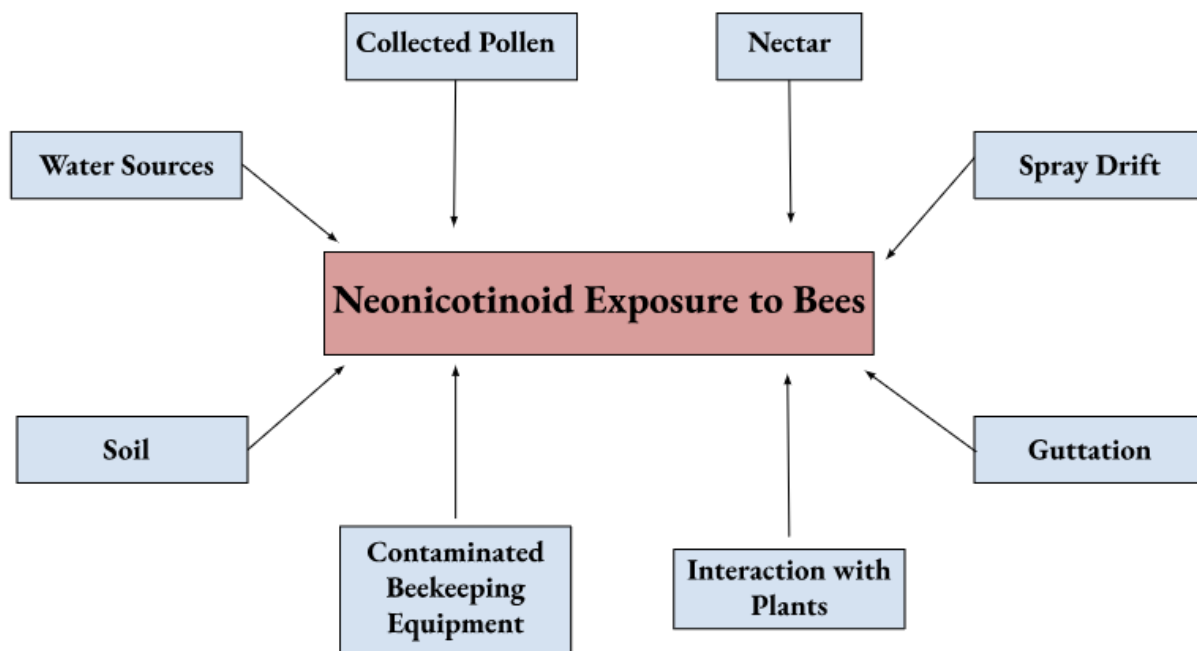
Figure 4: Different sources of neonicotinoid exposure to bees in agricultural settings.

Sublethal doses of neonics have been associated with reduced locomotion, transportation, foraging adaptability, learning, and olfactory response (observed in both field and semi-field settings)[88]. Field-realistic testing on the effect of neonics on worker bees finds reduced spatial awareness and avoidance of predators in affected individuals. Imidacloprid and clothianidin exposure has been shown to additionally negatively affect reproductive capability and the number of active bees in a hive, which is a predecessor to many forms of CCD[89]. Thus, there is a need to better understand the bio-physiological methods by which neonicotinoids affect the metabolism and homeostasis of affected bees.

The honeybee brain contains a variety of nAChR, promoted by the number of different possible subunits and alternative splicing during transcription[90]. However, the effect of imidacloprid is seen to be most adverse when binding to the heteromeric nAChR $\alpha 4\beta 2$ and the homomeric $\alpha 1$ and $\alpha 2$ receptors[91]. The limitation of signaling pathways has a wide variety of negative homeostatic effects on bees, as caused by the inability for signals to induce protein production and other cell functions at normal rates. Downregulation of various housekeeping genes in bees from CCD-positive colonies including vitellogenin (long-term memory), catalase (detoxification), and apidaecin (antimicrobial properties) corresponded to lower levels of cognition found[92]. The transcription of immune defense

proteins in particular, notably defensin-1, is reduced by the presence of clothianidin, as the neonic acts as a foreign kinase inhibitor in immune defense protein synthesis pathways[93]. In turn, a correlation is drawn between the reduced production of immune proteins [caused by neonicotinoid presence] and the presence of the parasitic mite *Varroa destructor*, indicating that the neonicotinoids play both a direct and indirect role in the occurrence of CCD. Various studies have pointed to decreased mitochondrial activity in the dorsal lobe and hypothalamus, as well as alterations to the brain lipidome in the presence of neonicotinoids; pathways including ribosome production, oxidative phosphorylation, nicotinate/nicotinamide oxidation were all altered[94]. RT-qPCR analysis reveals that various hormone-regulation transcripts, including farnesol dehydrogenase, were heavily downregulated in *A. mellifera*, while the lipoprotein apolipophorin-II like protein, was upregulated. Correspondingly, the lipid composition of select bee brains was changed and observed in accordance with reduced cognition and learning ability. In the honey bee *Apis cerana*, the lipid transport and storage protein typically found in the hypothalamus, Apolipophorin III, was downregulated in the presence of thiamethoxam, likely due to the insecticide acting as an allosteric inhibitor[95].

Changes to nuclear transcription have been stated in various studies, though few *direct* correlations between the variation in regulation and symptoms of CCD have been linked; it is more difficult to draw a direct causal relationship when discussing RNA transcripts given the complex post transcriptional changes that occur and various interaction with non-coding RNA. It should be noted that while a wide range of neonicotinoids' detrimental effects to bee species have been observed, certain species have somewhat of a natural defense against neonics of type N-cyano amidines (i.e. thiacloprid and acetamiprid): Cytochrome P450[96]; recognized for xenobiotic metabolism, P450 enzymes - especially CYP9Q3, and to a lesser extent, CYP9Q2 - have shown to provide limited protection to many insects from neonics with cyanoamidine functional groups (R-C≡N), including honey bees[97]. From their metabolic pathways, P450 enzymes possess the ability to convert limited quantities of neonicotinoids → glutathione. However, this oxidative process is substrate-limited, and thus is not as effective in dealing with chronic buildup of neonicotinoids, as it occurs in most real-life scenarios.

Given the extensive impact of neonicotinoids in relation to CCD, restrictions have been placed on the use of the insecticides in proximity to registered bee colonies; later sections outline the specific regulations. The linkage of neonics to different physiological aspects of bees has been for the most part well-described, although further recognition of the effect of RNA transcript regulation changes in needed to provide a more comprehensive view on the detrimental effects of neonics on bees. The example of bees speaks to a larger environmental concern about the changes that biotransformations and bioaccumulation of neonicotinoids can elicit in environments, as well as their effect on the balance of ecosystems.

Threats Posed to Humans

Pathways of Exposure

On the basis of the effects of neonicotinoids on non-target species, a growing number of concerns are being raised surrounding the detrimental effects of the insecticides in humans. Generally, neonics pose lower threats to mammalian species due to a lower affinity for nAChR subunits found solely (and abundantly) in mammals in comparison with insect-specific receptors[98]. However, cases of their toxicity, specifically following direct inhalation or consumption, have been the subject of various studies. Here, the sublethal and lethal effects of acute and chronic neonicotinoid exposure are discussed, and the molecular mechanisms by which neonics interact with nAChRs are discussed. The impact of reduced signal propagation on protein synthesis, cell regulation, and glucose metabolism, amongst other changes, are noted in cases of human exposure. Additionally, a note is presented on the presence of neonicotinoids in food, as well as the effects of the resulting bioaccumulation in the human body.

Neonicotinoids, like most insecticides, have a very low sorption coefficient, meaning stagnation occurs at ground level, where exposure to humans is higher. When exposed to neonicotinoids, metabolic and homeostatic changes are noted in tested subjects. There has been limited *in vivo* experimentation on the modes of entry for neonicotinoids into humans given the toxic effect in higher quantities. Limited studies find a host of potential exposures, with agriculture as a primary source of neonic uptake. An analysis of 173 studies from 1988 to 2022 found surface water contamination as a result of neonicotinoid adhesion to surface water pollutants and leaching were major sources of entry into agricultural land water supplies[99]. In water, neonicotinoids are susceptible to degradation pathways through both bulk water hydrolysis and microbes. Recently, biomonitoring of pesticidal and specifically, insecticidal presence in humans has moved towards urine sampling, as intact insecticides are far harder to track through traditionally used bioassays. The presence of cyclic urea, 6-chloronicotinic acid, and N-methyl-thiamethoxam in urine samples of individuals exposed to contaminated well water suggest the same, as found by Thompson et al[38]. Another urine-excretion sampling found the presence of acetamiprid and thiamethoxam in human urine following routine insecticidal applications on agricultural land[100]. A positive, causational link was determined between the quantity of neonicotinoids applied (and thereby, exposed to) and the quantity of acetamiprid and thiamethoxam found in the selected urine samples (0.13μg per 100g applied, $p < 0.05$). Seccia et al. [2005] determined through liquid chromatography-mass spectroscopy that while testing for a 100 μgL^{-1} presence of neonicotinoids in public drinking water, acetamiprid, imidacloprid, thiacloprid, and thiamethoxam were found at average levels of 102, 87, 101, and 89 μgL^{-1}, respectively[101].

Nomura et al. [2013] identified the presence of dinotefuran, 6-chloronicotinic acid, and its conjugate 3-furoic acid in a sample of Japanese farmers' urine[100]. Deconjugation using metabolites and glucuronic acid revealed the further presence of imidacloprid and thiamethoxam, both of which were part of the maize seed coatings being used by the samples. In a similar sampling, the presence of the neonicotinoids thiamethoxam, thiacloprid, imidacloprid, clothianidin, acetamiprid, nitenpyram, and dinotefuran (in decreasing order of concentration) were identified in >50 Japanese samples with prior history of neonicotinoid spraying applications. The same experimental analysis finds an increase in the levels of clothianidin reported in sampled women when compared to an earlier 1994 experiment. Furthermore, the presence of imidacloprid and thiamethoxam in the 2011 study were not present in the findings of the earlier experiment. A potential explanation for this change is over this time period, neonicotinoids rose in popularity compared to organophosphorus compounds and carbamates, becoming the most widely used class of insecticides in Japan.

For non-agricultural-based individuals, exposure to neonicotinoids remains limited. Regardless, a number of studies aimed to identify the trends in neonics in food products have noted minute quantities on or in vegetable products, bovine milk, leafy greens, and other consumable items. The United States Department of Agriculture estimates imidacloprid in 81% of sweet bell peppers and broccoli and 57% of grapes produced in the US. Further, ~46, 30, 24, and 21 percent of cherry, apple, pear, and strawberry samples, respectively, collected from nationwide United States samples suggests persistence of acetamiprid in a systematic nature[9]. In tested leafy greens (kale, spinach, and cilantro), the same study indicates maximum residue levels of 1.4-1.6 acetamiprid parts per million. Residue data characterized for daily dietary intake of neonicotinoids found the presence of more than one neonic in over 90% of bovine milk used for human consumption[102]; tested Chinese milk possessed medians of 0.1 - 3.1 μgL^{-1} for acetamiprid, N-desmethyl acetamiprid, and imidacloprid. The geographical techniques used for farming in northwestern China were identified as primary causes for the increased contamination; inorganic farming paired with elevated levels of neonicotinoid applications prove to be sources of entrance into bovine water and feed. While these and other studies support the idea of urban exposure through food contamination, the quantities of exposure remain far lower than in agricultural settings, and there has been little evidence of noteworthy changes in metabolism or homeostasis in humans.

Unfortunately, an ongoing challenge is neonicotinoid poisoning through consumption in highly toxic quantities. Over a hundred cases of fatal neonicotinoid-related poisonings have been observed, cumulative of mainly ingestion of branded insecticides[103]. As such, governmental regulations on the use of the insecticides have been modified, though special provisions vary from region to region. Unlike carbamates, organophosphates, and organochlorine compounds though, the toxicity of neonicotinoids is relatively smaller, with only <2.9% of attempted ingestion resulting in death (differences in medical treatment considered)[103]. Barring intentional ingestion, occupational hazard,

and dietary exposure (including honey), the mechanisms by which humans interact with notable levels of neonics.

Molecular Action & Physiological Effects

Initial approval for the use of neonicotinoids was based on the premise of affinity to mostly/solely to insect nAChRs; however, recent research has identified a host of negative effects in humans at sublethal doses[104]. Neonicotinoids are found to be most effective against $\alpha4\beta2$ acetylcholine receptors, which comprise the majority of insect acetylcholine receptors, but only a fraction in humans[105]. However, this receptor is found in an elevated spatial concentration specifically in the thalamus region of the brain. Exposure to neonicotinoids in humans acts as a competitive inhibitor with acetylcholine, vying for binding space on acetylcholine receptors. However, the inability for effective hydrolysis by acetylcholinesterase means successive electric propagation and overstimulation. *In vitro*, a 300 μM solution of clothianidin was observed to have a similar effect to a 2 mM concentration of acetylcholine on the $\alpha4\beta2$ receptor[106]. A similar result was observed for imidacloprid and thiamethoxam, indicating a high affinity for the protein, although demonstrating a lower efficacy than nicotine. Accordingly, acute exposure to neonicotinoids as described in field studies cause mild overstimulations of not only $\alpha4\beta2$, but also $\alpha7$ homomeric receptors on the basis of interactions between hydrophilic regions[5]. Again, lower efficacy in comparison with insect nicotinic acetylcholine receptors are observed.

Toxicity has been described mainly on antagonistic action on the $\alpha4\beta2$ receptor; this receptor is implicated in learning and following post-synaptic excitation, permeability of Na^+ and K^+ ions[107]. In human cases, there have been no recognized antidotes for neonics and their antagonistic action, disrupting homeostasis[108]. Here the effects of the mild abnormal signaling on both normal signal propagation and protein activity is discussed.

In vitro genotoxicity of human blood lymphocyte cells was observed in a linear fashion following thiacloprid, clothianidin, and imidacloprid applications[109]. When applied in high concentrations (10x sublethal constant), >80% of nuclear DNA was observed to have damage at ends of helices, acting as oxidative reagent, and tail shortening. Genetic instability through the formation of micronuclei and exchanges between sister chromatids during cell division was also identified. Such mutations have been linked with oncogenesis and improper gene transcription[110]. In samples containing over 1000 individuals, patients identified with exposure to one or more neonics experienced medically significant outcomes, including chest pain, nausea, red eye, inflammation, headache, dizziness, and dermal irritation, amongst others[111]. The most serious outcomes described were hypertension and tachycardia (<1% of samples), although neither of these symptoms prolonged and dissipated within 10-15 hours post-ingestion. An observational study by Mohamed et al. [2009]

found in 56 self-ingestion cases found similar results in patients post-ingestion[112]. A 70-patient analysis of cases of self-ingestion reported to the Taiwan Poison Center in 2009 reported that in addition to the mentioned symptoms, in 57 patients, mild muscular tetanus and paralysis of connective muscles were described[113]. The root cause was identified as the overstimulation of acetylcholine receptors in the hypothalamus, which in turn propagates neural signals to neuromuscular junctions. Keil, Daniels, and Hertz-Picciotto [2014] described the conjunction between early life exposure to neonicotinoids, specifically imidacloprid, and the development of autism spectrum disorder retrospectively[114]. An odds ratio of 1.3 was determined for early life (blastula stage) exposure to imidacloprid and chances of developing autism when compared to a control. A negative regression model was described at a 95% confidence interval between trimester and exposure to neonics against odds of developing autism. It should be noted that the disorder is caused by a host of genetic and neural differences, and the study presents a non-causational relationship that simply describes a trend. A 2014 observational study found out of 101 case studies, 38% of cases of offspring contingent heart defects could be attributed in part to the influence of neonicotinoids. Specifically, the limitation of genetic development through instability was noted in mid-pregnancy reports, and resultantly, a number of offspring were born with coarctation of the aorta (n = 74), hypoplastic left heart syndrome (n = 59), or ventricular septal defects (n = 93). Yang et al. examined the same sample data for neural tube defects and found that offspring whose mothers resided within a 500m radius to a pesticidal application location were at significantly higher risk of developing anencephaly, spina bifida, or cleft palate[115].

While many other articles of research suggest similar sublethal or lethal effects of neonicotinoids (depending on the quantity exposed to or ingested), it is important to recognize limitations in determining neonics as a singular cause of varying phenotypes, and moreover, identifying neonics *in vivo*.

Bans & Restrictions on Neonicotinoid Usage

Given the varying environmental and toxic effects of neonicotinoids described in non-target species, there is a growing movement to restrict and/or outright ban the use of them for agricultural or urban uses. Here, legislation regarding the restriction of neonicotinoids is discussed for three leading regions of usage/production of the chemicals.

Europe

The 2004 Stockholm Convention placed flat bans on the use of organochlorines including DDT, HCH, and lindane, recommending neonicotinoids (amongst others) as a more specific,

environmentally-conscious choice. However, finding on the sublethal and lethal effect of the insecticides on bees, aquatic organisms, and certain amphibians created push-back against their use. In 2009, Italy became the first European country to pose limitations on the application of neonicotinoids; its use on maize in the form of foliar sprays and seed coatings was completely outlawed[116]. The United Kingdom and France followed suit with restrictions being placed on the use of imidacloprid in agricultural settings with high pollination activity. The European Union (EU) began to recommend organic alternatives to neonicotinoids in the 2010s due to rising concerns of the effect of neonicotinoids on non-target species, with a special note on the acute presence of neonics in maize (EFSA). Three years later, the EU heavily restricted the use of seed coatings containing clothianidin, thiamethoxam, and imidacloprid, which were the leading insecticides used at the time[117]. The restriction was placed on pollinator-attracting economic crops, including maize, oilseed rape, and sunflower following a judgement that the insecticides posed a credible threat to non-target insect species, notably bees. A confirmatory hearing was made in February of 2018, expanding the restrictions to non-greenhouse, outdoor uses in all EU nations. The decision comes on the back of a call for the continuation of neonicotinoid usage in the farming community given its economic importance. Temporary derogations were granted in France based on new provincial, agricultural laws in 2020, granting special access to both imidacloprid and thiamethoxam[118]. Applications authorized both seed coatings and systematic spraying on a free range of economic crops, including maize, soybean, and other pollinator crops. However, the temporary lift of the ban was revoked in 2023 following a tertiary hearing by the European Union. Thus, neonicotinoids are authorized for application only on non-pollinator crops, as directed by the EU's food and safety organization, EFSA. In addition, the export of neonicotinoids - once a primary pesticide produced in Europe - has been restricted through the form of tariff and trade regulation requirements.

North America

Neonicotinoids are not subject to strict federal restrictions in the United States as it relates to application method, but statewide policies vary in their leniency towards its usage. Many states, including Minnesota, New York, Nevada, and Colorado have moved to ban the use of neonicotinoids on conservation land, further regulate the labeling of pollinator-friendly economic crops, and limit the use of neonics in seed treatments[119]. Furthermore, state regulations on urban usage on lawns, fields, and outdoor settings have been enacted. Regardless, the United States Environmental Protection Agency maintains that neonicotinoids are still a recommended insecticide in dealing with nematodes, thrips, aphids, beetles, and other pests. An initial ban on neonicotinoids existed in all provinces of Canada from 2010 to 2021, citing environmental dangers from runoff and aggregation in water sources. However, Health Canada reversed this ban in 2021. Imidacloprid, thiamethoxam, and

clothianidin are permitted under new federal regulations to be used in foliar sprays and pollinator-friendly seed coatings. In agrarian North American communities, such as those found in parts of Latin America and Mexico, regulations on neonics are sparse, and the class continues to be the most widely used group of insecticides[120].

Asia

In other agrarian states, regulation on the use of neonicotinoids continues to be sparse. Asian nations, including India, China, and Indonesia, continue to be some of the leading consumers of imidacloprid, thiamethoxam, acetamiprid, and clothianidin in seed coating, sprays, and powder applications[118]. This is the case for urban applications as well, where neonics are used primarily in targeted control of thrips, cockroaches, moths, and other related pests. The low effective dosages of neonicotinoids in comparison with organophosphates, organochlorines, carbamates, and pyrethroids - major classes of economic insecticides - allow for limited regulation and restrictions. In turn, environmental damages in the form of surface runoff, groundwater contamination, and disruption of aquatic and terrestrial ecosystems have been noted in greater quantities in India and China[121]. In India, the only federal restriction placed on neonics was a temporary ban on imidacloprid and its relative fipronil in 2018 due to toxic effect on non-target species, including bees and other pollinators. However, the ban was overturned following several protests citing the importance of neonicotinoids in farming communities as an effective measure to displace pests. Currently, limited legislation is proposed in Indonesia and China to restrict the use of neonicotinoids on pollinator-friendly plant species, including maize and soy.

Future of Neonicotinoids

Neonicotinoids continue to remain the most widely-used class of chemical insecticides worldwide and will likely continue to remain so for the next decade. Their main advantages over comparable insecticide classes are the increased [insect] specificity and cheaper cost of production. Furthermore, while organophosphorus compounds, organochlorines, pyrethroids, and carbamates all are measured in kilograms per acre, neonics are one of the first groups of insecticides with application quantities in the grams per acre. This property is not at the cost of effectiveness, as similar class comparisons yield equally similar LD_{50} ranges. Specific soil pests, including white grubs, roundworms, and earthworms, are more easily contained through the use of neonics in systemic applications, contrasting the excessive quantity of either organochlorines or organophosphorus compounds needed prior. Imidacloprid, thiamethoxam, and clothianidin lead applications of insecticides on sugarcane,

maize, soy, and other stalk plants, and cover over 150 million acres of land in the United States (leading user globally) alone.

However, the environmental risks associated with neonicotinoids – and for that matter, all major insecticide classes – are concerning for both their impact on humans in close proximity to their application and other non-target species, notably honeybees. A new movement of eco-friendly farming techniques are on the rise, limiting the use of chemical insecticides, fertilizers, and other agrochemical techniques or substances, with the intention of a more sustainable and environmentally conscious crop production cycle. The use of microbial insecticides – bacterial communities which produce biotoxins with insecticidal properties – has also gained traction. The most widely used microbial insecticide is of the crystalline (cry) protein family from the gram-positive *Bacillus thuringiensis*, which binds to glycosyl-phosphatidyl-inositol anchored ALP or APN receptors in insect midgut or posterior regions[122]. The main advantage of a microbial insecticide over a chemical insecticide is the heightened target specificity with little to no risk of negative impact on non-target species; proteins synthesized from 'insecticidal microbes' have 3D structures fit for the structure of insect midgut (or other target) receptors specifically, which differ greatly in spatial configuration with human and mammalian receptors of similar function. Unlike such receptors, nAChRs, the target receptor of most chemical insecticides, shares many analog similarities in mammals and insects, thus explaining the impact on non-target species. In addition, a new generation of chemical insecticides, mainly composed of anthranilic diamides, are underway in trial and production[123]. The potential of alleviating the environmental risks associated with neonicotinoid usage is a prospect gaining traction in both agricultural and legislative settings, being set a precedent of new agricultural and insecticidal technology.

While alternatives to neonicotinoid [and chemical] insecticides are an exciting and upcoming area of research and a potential new frontier of maintaining crop output, their tangible applications are still limited. Bioinsecticides are extremely specific in their target and thus cannot be used against a wider range of feeding insects like neonicotinoids. Microbial insecticides from *B. thuringiensis* or other members of the Bacillus family (which produce Cry proteins and homologous substances) must additionally be stored in extremely cold temperatures and applied in quantities far greater than required for effective neonicotinoid applications. As a result, the economic advantages of neonicotinoids over both newer and older classes of insecticides have been a primary reason of their continued success. In developing nations, the monetary benefits of selecting and using a cheaper insecticide such as imidacloprid over more expensive bioinsecticides (also limited by availability) is often a large factor in deciding which insecticide to purchase. As for organochlorines, organophosphorus compounds, carbamates, and pyrethroids, existing legislation set forward regionally

and globally (e.g. Stockholm Convention, 2004) have limited their ability to compete with neonicotinoids.

It is key that neonicotinoids, given their advantages, are used sustainably with the larger effects on the environment in mind. Applications must be mindful of the presence of surface water bodies, groundwater sources, or large numbers of non-target species within radii of usage. Proper farming technique (weather forecasting, spray broom down, etc.) in preventing spray drift has additionally shown to reduce exposure to non-target species, including those that interact with plants where neonicotinoids are applied[124]. A special note to bee colonies in the vicinity of application when considering use may help mitigate chronic exposure to neonicotinoids and its negative effects. Regular tracking of water quality and leaching of insecticides into bodies would indicate both the safety of the water for consumption/use as well as the quantity of runoff. If such factors are maintained, *ceteris paribus*, environmental damages of neonicotinoids can be reduced. Thus, the future of neonicotinoid usage is dependent on the advent of new insecticidal technologies, legislative restriction, and maintaining of proper safety practices when dealing with the insecticide. Only time will tell whether or not neonics will continue as the most widely used chemical insecticide.

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Lightweight Website Classification by DOM Features

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ABSTRACT

Website classification methods are largely based on generic text classification techniques. We present an experiment that leverages web-specific features relating to the document DOM (Document Object Model) structure to obtain better classification results in comparison to generic methods. The methods presented in this paper are based on clustering in embedding space. Such methods can minimize computing resources and data size as a lightweight alternative compared to other cutting-edge generative AI methods. By using these methods and with the help of web-specific features we are able to show results on par with those of advanced models, such as BERT in classifying websites with half a percent variation in accuracy, and we show how we arrive at optimal results by choosing the desired parameters. Our method surpassed results reported by models such as Random Forest Classifier, Linear SVC, Multinomial Naive Bayes, and Gaussian Naive Bayes.

Keywords: web page classification; clustering; categorization; embeddings; text classification; deep learning; KNN; BERT; OpenAI

1 BACKGROUND

Web classification has many important applications. In cybersecurity and compliance, the technology can be used to provide businesses with web filtration of

certain website categories, block sites potentially containing malware or phishing websites, or be used for parental control. Other applications include recommendation engines where utilizing multimodal embeddings can be used to improve the results. Another potential application of this technology is for business intelligence (BI) when it comes to finding and comparing similar products or companies. For example, consumers searching for products online can find the competitors who offer the most similar services for the lowest cost.

The classification problem of text documents has been studied extensively. We can describe the problem in the following way:

> Given a corpora C with n document classes $C = \{D_1, \dots D_n\}$, and given a document d, assign it to one of the classes $C_1 \dots C_m$

The classification of web pages is a special case of the text classification problem. Web classification is important for many use cases including filtration of dangerous

content such as phishing websites, offensive content, or content that violates corporate security and policies, such as gambling or malware, and many other use cases. We will first briefly summarize some of the key methods for general text classification and then suggest some enhancements for web classification.

We focus on supervised learning, which is a type of machine learning involving training a machine learning model on a labeled dataset, where the algorithm learns to make predictions or classifications based on input-output pairs. In this case, the input is a corpus of HTML documents and the labels are the categories that we express as integers (for example, we would like a web page from amazon.com to be classified as category 3, which is e-commerce).

1.1 Bayesian models

The Naive Bayes model uses a posterior probability of the keywords to determine the category, C_{NB} as a common method for classification of text . Let $C = (C_1...C_m)$ be m document classes and let a document D have a word list $W = (W_1...W_{d'})$ is assigned:

$$C_{NB} = argmax_{c_j \in C} P(C_j) \prod_{i=1}^{d'} P(W_i \mid C_j)$$

(Jurafsky and Martin)

1.2 Random Forest Model
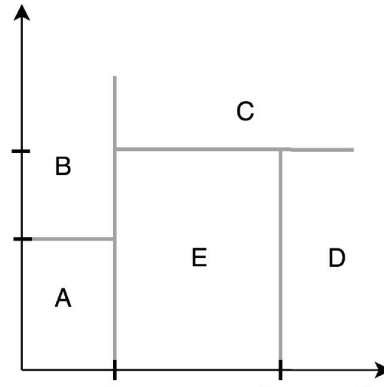
Figure 1: Decision regions created by an ensemble of decision trees (Schonlau and Zou 3-29)

Random Forest Models find the best partition of the space into the desired clusters, where each partition starts randomly and is built using a decision tree, such as in Figure 1 above. These decision trees recursively partition an input space into subsets based on different characteristics of the input, which subsequently creates a hierarchical structure resembling a tree.

1.3 Neural Network Models

A neural network model is a computational model drawing from the neurons of the human brain. The basis of a neural network is layers of interconnected nodes (or neurons) each assigned with weights, as depicted in Figure 2.
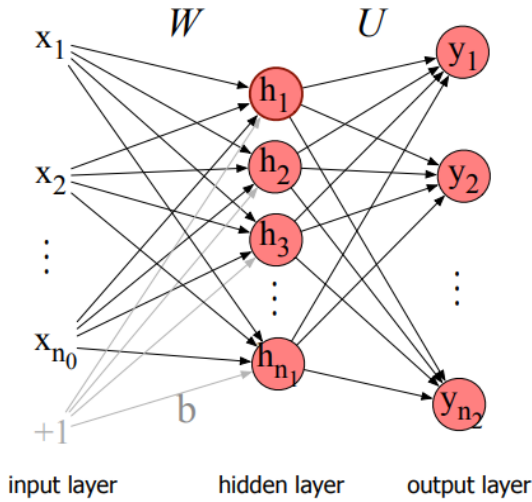
Figure 2: Example diagram of a 2-layer feedforward network (Jurafsky and Martin)

Neural networks use a process called "backpropagation" which computes the gradient of the error function with respect to each of the weights. The model adjusts its weights until it can predict the desired outcomes.

1.4 BERT
Introduced by Google in 2018, BERT, or Bidirectional Encoder Representations from Transformers, uses a deep neural network transformer architecture (Vaswani et al.) to reflect contextual relationships between words bidirectionally in a given text. BERT's training on vast corpora has enabled it to grasp linguistic nuances in varying contexts. The BERT transformer model is shown in Figure 3, whereby the left encoder part is primarily utilized for BERT.
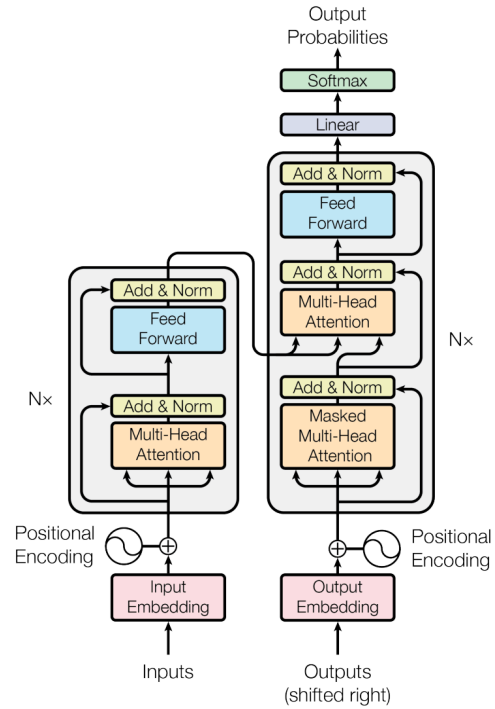
Figure 3: Transformer deep neural network architecture as used in BERT

2 METHODOLOGY
For this research, we chose a corpus of HTML web pages taken from a Kaggle data set containing a labeled data set of URLs and categories (Business, Travel, Games, News, Sports, Food, and others). We scraped over a thousand web pages and transformed the HTML code to its embedding space, so we could achieve a metric that is based on semantic similarity of the words in each web page. We used OpenAI's API with the Ada-2 engine which is superior to previous work done with Word2Vec to generate a 1,536-dimensional representation of each page. We then further take these high dimensional vectors in embedding space and we weigh them based on the page's HTML DOM structure. This way we can assign different weights or priorities to vectors that represent more important parts of each page.

We then split the data into training and test sets and perform KNN (K-Nearest Neighbor) clustering to determine the closest cluster or category for each page based on the cosine similarity metric in embedding space. Finally, we compare our results using a variety of different parameters, such as different weights, stop word elimination, and values of K, and further compare our results to existing research. We chose this method as a lightweight technique that doesn't require massive data sets, CPU, and memory resources, as required by a transformer network such as BERT.

Step 1 Transformation to Embedding Space
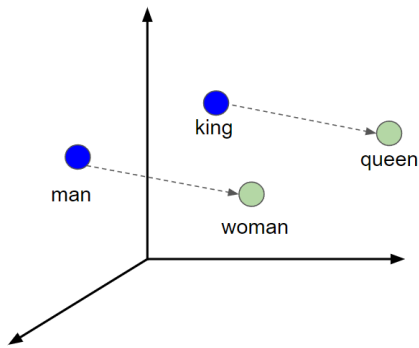
Figure 4: Male-female relationship in embedding space

In this context, an embedding space is a mathematical space in which words are expressed as vectors. Semantically similar words are positioned close to each other in this space as seen in Figure 4 to capture relationships between each other. The distances and directions between these vectors capture semantic relationships between words. The distance metric can be expressed through Euclidean distance which

is a function of two points in n-dimensional space,

$$d(p, q) = \sqrt{\sum_{i=1}^{n} (q_i - p_i)^2}$$

or cosine distance,

$$cos(\Theta) = \frac{P \cdot Q}{||P|| \, ||Q||} = \frac{\sum_{i=1}^{n} A_i B_i}{\sqrt{\sum_{i=1}^{n} A_i^2} \sqrt{\sum_{i=1}^{n} B_i^2}}$$

(Augustin and Porter)
Embedding spaces are learned through training algorithms on expansive datasets, allowing the model to understand and represent the underlying patterns and similarities in the data.

In a preprocessing step before vectorization, the HTML is extracted by tags, relative importance, and is cleaned of stop words. Stop words (i.e. "the," "for," or "could") are words that are filtered out during this step due to their high frequency and low informativeness.

Step 2 DOM Feature Weighting

We would like to use the metadata embedded in HTML documents, i.e. the HTML tags to help us weigh the document features to achieve the best classification. For example, a <title> or <h1> tags most likely are more pertinent to classification than a <p> tag. We therefore are looking to define a vector,

$$V = \sum \frac{\alpha_i v_i}{\sqrt{\alpha_i^2}}$$

Whereby α_i are the coefficients weighing different priority HTML tags to express

them more strongly when calculating the distance.
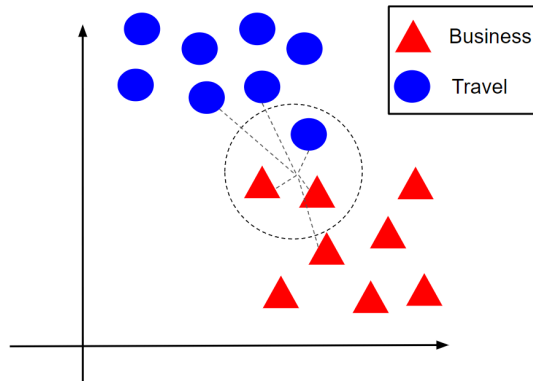
Step 3 k-Nearest Neighbor Classification

Figure 5: KNN classifying neighbor points (k=3)

In the experiment, we partitioned 30% of the data set for the test set and used 70% as the training set with varying values of K. Figure 5 shows an example of KNN using the categories Business and Travel to see which are most similar to each other as "classification is achieved by identifying the nearest neighbors to a query example and using those neighbors to determine the class of the query" (Cunningham and Delany).

Step 4 Measuring Outcomes

Baseline results
Below are results based on averaging of 3 trials for different values of K:

	K = 5	K = 3	fold_idx
Accuracy	88.44%	90.17%	1
Precision	90.08%	91.98%	1

We finally calculate the accuracy, precision, recall, and F1 score which are metrics commonly used to evaluate the performance of classification models. These metrics offer nuanced insights, crucial in scenarios with imbalanced class distributions.

3 RESULTS

3.1 Baseline Classification
In this trial, we use the extracted text from the websites, remove stop words, and perform embeddings with OpenAI followed by KNN clustering.

The initial experiment established a baseline for classification based on the KNN and embedding techniques without weighing any web-specific features. One of our first metrics to decide was which value of K worked best and generally optimized the total accuracy. Using the baseline comparisons where the only variable changed was K, we found the K = 3 was sufficient for our purposes. With every run, we generated metrics such as seen in Table 1, and created a confusion matrix with a color spectrum representing accuracy per category for visualization.

Recall	88.44%	90.17%	1
F1 score	88.62%	90.50%	1
Accuracy	87.86%	89.60%	2
Precision	90.63%	91.02%	2
Recall	87.86%	89.60%	2
F1 score	88.52%	89.81%	2

Accuracy	90.75%	91.91%	3
Precision	92.21%	92.93%	3
Recall	90.75%	91.91%	3
F1 score	90.85%	91.92%	3
Accuracy	89.02%	90.56%	Average

Precision	90.97%	91.98%	Average
Recall	89.02%	90.56%	Average
F1 score	89.33%	90.74%	Average

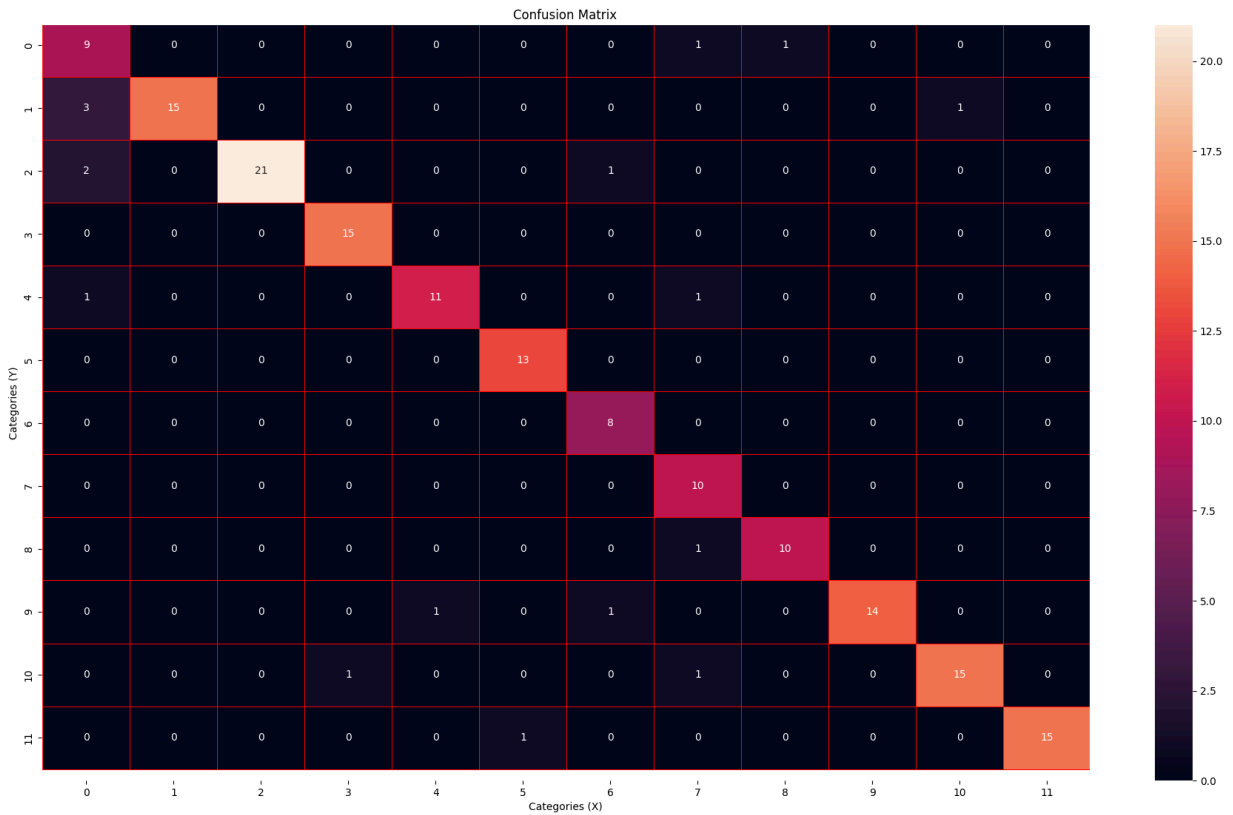Table 1: Samples of each K using regular KNN text-based classification trial

Figure 6: Sample confusion matrix for regular text classification with for fold_idx = 1, k = 3
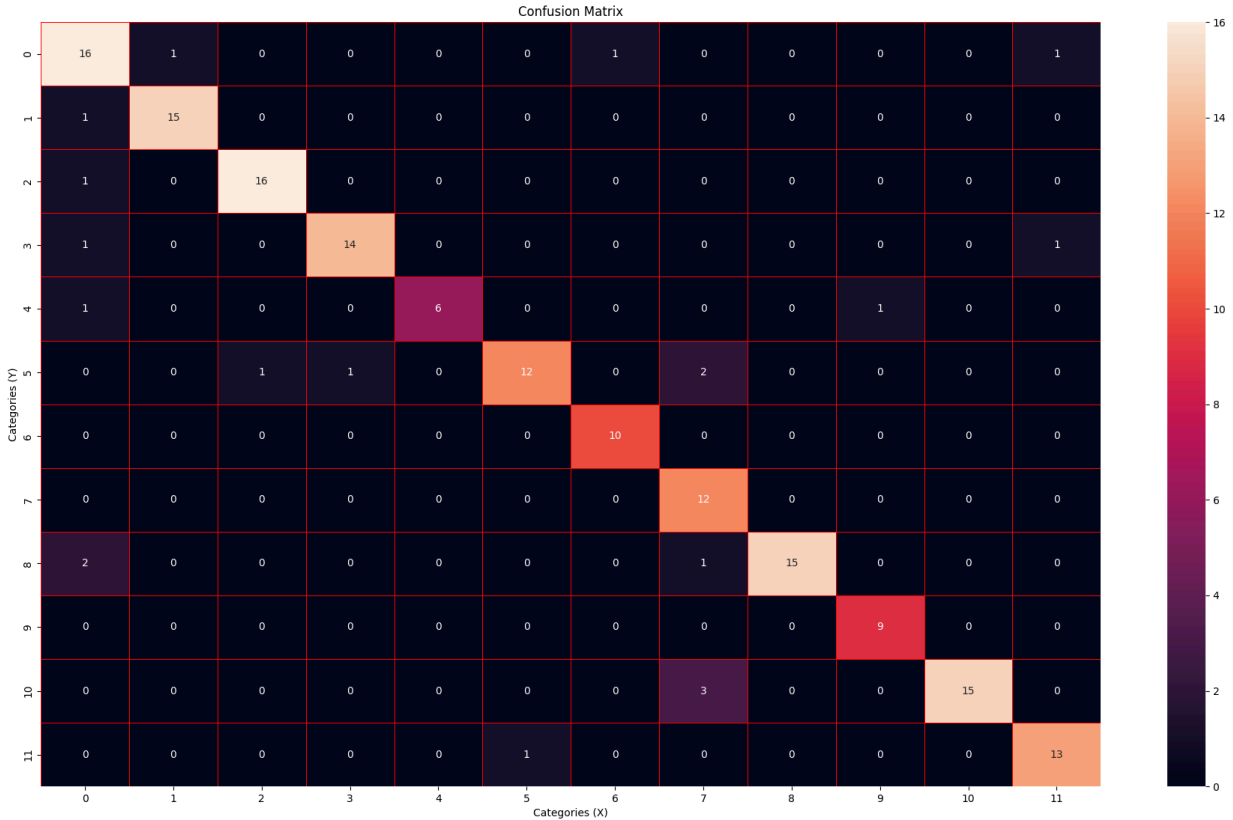
Figure 7: Sample confusion matrix for regular text classification for fold_idx = 1, k = 5

3.2 Classification incorporating DOM features

We improved the baseline results by using a scalar to increase the magnitude of vectors associated with more important pieces of text based on DOM structure. The weighting combination which gave the best results had each DOM group of elements at 1x, 2x, and 3x the original weight, or in other words, we chose a, b, and c = 1 as coefficients for $aV_1 + bV_2 + cV_3$ weighing the embedding vectors associated with the standard text in <p>, <div>, and <span> tags, more important text in headers <h1>, <h2>, <h3>, <h4>, <h5>, <h6> and the most impactful information in <title> and meta description tags.

Weight coefficients (1, 1, 1), k = 3

Accuracy	94.80%	1
Precision	95.50%	1

Recall	94.80%	1
F1 score	94.87%	1
Accuracy	95.38%	2

Precision	95.97%	2
Recall	95.38%	2
F1 score	95.52%	2
Accuracy	93.64%	3
Precision	94.25%	3
Recall	93.64%	3
F1 score	93.72%	3

Accuracy	94.61%	Average
Precision	95.24%	Average
Recall	94.61%	Average
F1 score	94.70%	Average

Table 2: Results from text-based classification trial
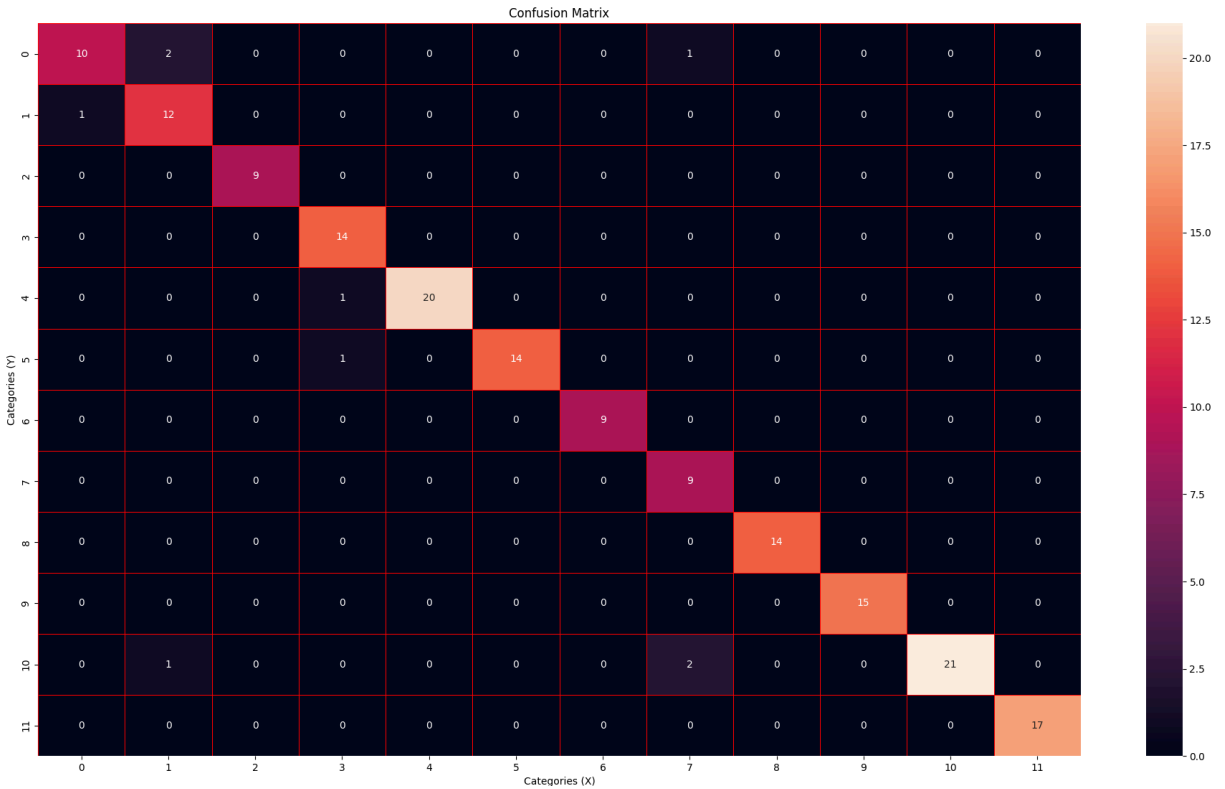
Figure 8: Sample confusion matrix for DOM-weighted text classification for fold_idx = 1, k = 3

4 ANALYSIS

Comparing our results using the DOM-weighted KNN method, we see that we surpassed methods including Random Forest Classifiers, Linear

SVC (Support Vector Classification), Multinomial Naive Bayes, and Gaussian Naive Bayes as shown in Table 3. Moreover, our method was on par with the BERT version, RoBERTa, which uses a massive pretrained language model in contrast to our lightweight embedding space approach. We see high accuracy of our method, and in fact if we examine the data we can see that the errors are in fact errors we believe humans are prone to making as well. For example, mistaking a sports news article and a generic news article when it comes to selecting between the Sports and News category or whether a business website with an online component should be categorized as Business or E-Commerce. As such, we believe even a human would not achieve significantly better results.

In terms of performance, we believe our technique does not require a large corpus, or significant memory or compute resources, in contrast to BERT. Moreover, when encountering new data our method automatically learns and improves as the data is clustered and added to its mode, whereas BERT would require separate training or finetuning and these steps typically require costly hardware and GPUs.

4.1 Comparative Analysis

model_name	fold_idx	accuracy
RandomForestClassifier[1]	0	0.719858
RandomForestClassifier[1]	1	0.751773
RandomForestClassifier[1]	2	0.716312
RandomForestClassifier[1]	3	0.736655
RandomForestClassifier[1]	4	0.679715
LinearSVC[1]	0	0.858156
LinearSVC[1]	1	0.932624
LinearSVC[1]	2	0.939716
LinearSVC[1]	3	0.903915
LinearSVC[1]	4	0.879004
MultinomialNB[1]	0	0.812057
MultinomialNB[1]	1	0.879433
MultinomialNB[1]	2	0.872340
MultinomialNB[1]	3	0.882562
MultinomialNB[1]	4	0.818505
GaussianNB[1]	0	0.702128
GaussianNB[1]	1	0.762411
GaussianNB[1]	2	0.780142
GaussianNB[1]	3	0.754448
GaussianNB[1]	4	0.644128
DOM-weighted KNN	Avg	0.9461
RoBERTa[2]	N/A	0.9504

Table 3: Comparison of other methods (1. Loro) (2. Mehta) with our DOM-weighted KNN method accuracy from Table 2

5 FUTURE DIRECTIONS

5.1 Positional encoding
We would like to try adding positional encoding, such as used by transformers and by BERT. For example, we add the following to the vectors used for clustering:

$$PE_{(pos,2i)} = sin(pos/10000^{2i/d_{model}})$$

$$PE_{(pos,2i+1)} = cos(pos/10000^{2i/d_{model}})$$
(Vaswani et al.)

With positional encoding, we assume more semantic relationships between keywords will be taken into account by our metrics, as vectors representing similarly positioned words will match more closely.

5.2 Using N-grams
We would like to try clustering by pairs, triplets, or n-grams, thereby providing additional semantic relationships between sentence parts rather than individual tokens.

5.3 Incorporating BERT
By incorporating DOM features into BERT pretraining we hope to achieve the best of both worlds and achieve the highest level of semantic understanding for classification.

6 ACKNOWLEDGMENTS

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Biomimetics- The Key to Better Space Suits

Abstract

Current space suits are expensive, bulky, and hard to maintain. Space exploration will significantly benefit from advancements in space suit technology that allow for increased safety and mobility. Using biomimetics, implementing bio-inspired adaptations of flora and fauna into technology emphasizes the possibility of enhancing our modern-day space suits and revolutionizing the exploration of outer space. Here, we review the current challenges of space suits to form a baseline and better understand the limitations of space suits. The investigation underscored four significant concerns in space suit technology for space exploration: Radiation, thermoregulation, debris protection, and maneuverability. The research showed that biomimetics can be a powerful resource to model the next generation of space suits, resolving problems around radiation, thermoregulation, debris protection, and maneuverability. The research shows various flora and fauna with these characteristics and demonstrates potential for practical application. In conclusion, the research findings highlight the benefits of biomimetics in modern space suits.

Introduction

Space exploration is an arduous challenge that demands advanced technologies and equipment to ensure astronauts' well-being and safety in space. Space suits play an integral part in space exploration by protecting from space's harsh environment; however, current space suits have several shortcomings that restrict long-term exploration, radiation protection being of primary concern. Current space suits only offer enough protection for short-term living. NASA is exploring various techniques and technologies to mitigate radiation exposure during space travel.

Thermal protection in space suits needs improvement as its multiple layers impede astronauts' movements, making it harder for them to complete tasks outside their spaceship. Mobility is key for astronauts' quality of life as it will allow them to complete tasks outside the ship much more easily than with current space suits. Protection from micrometeoroid debris is also crucial, as they orbit Earth quickly and pose a high risk of colliding with astronauts. Innovation of space suits will be integral for successful long-term space exploration. Space suits need improvement for humanity's long-term interests in space exploration. Radiation protection is needed due to space's many health risks.

Biomimetics

Biomimetics, or imitating biology, is the study of using nature's designs as inspiration to advance space-suit technology for exploring space. Biomimicry has already been applied in some problem-solving efforts within space programs worldwide. Here are a few uses of biomimetics when designing space suits:

Design Inspiration: Biomimetics can serve as an avenue for space suit design inspiration, drawing from designs found within nature as sources.

Material Selection: Biomimetics can help select materials for space suits, using materials found in nature as inspiration to develop new space suit materials (for instance, spider silk as potential space suit material)

Functionality: Biomimetics can help enhance the functionality of space suits by drawing inspiration from nature for improving mobility and flexibility, such as imitating jellyfish movement as an example for improving mobility in space suits6

Biomimetics provides us with an effective means of creating space suits that are both efficient and sustainable, perfect for long-term exploration in space. By studying nature as our inspiration, we can develop spacesuits that offer greater performance & functionality for longer space exploration missions.

Several lifeforms on Earth can maintain thermoregulation even in extreme climates like space. The ever-growing debris in space poses a daunting obstacle that lightweight and flexible suits that allow an unrestricted range of motion will combat. Maneuverability poses essential criteria for the success of a space suit to enable the astronaut to have a more extensive range of movement outside of the shuttle to make repairs and conduct experiments. Although human civilization is only about 6,000 years old, nature has been changing and adapting to its surroundings for billions of years. Nature has developed efficient and effective solutions to various challenges over time, and these solutions can be studied and applied to improve technology, including space-suit technology. By studying the natural world, we can gain insights into how to create more sustainable and effective space suits that can help us explore and utilize the near-unlimited resources of space. Biomimetics is a field of study that involves learning from nature by imitating or taking inspiration from nature's designs and processes to solve human problems.[1]. This paper focuses on the emulation of biology and how we can use nature to advance space-suit technology to expand our horizons and use the near-unlimited resources of space.[2]

Protection from Radiation

1. Dangers of radiation [3]

Protection from radiation is imperative if we wish to travel into space. The lack of radioprotective space suits hinders the production of new cells in the brain. At the rate the body degrades due to amounts of radiation, the lack of neurogenesis can lead to reduced memory or brain damage. Radiation has catastrophic consequences on the cardiovascular system. It narrows arteries and removes the

lining of the blood vessels, which causes several diseases. Radiation has the most significant impact on the DNA of humans. The four bases, guanine, cytosine thymine, and adenine, can easily be mutated, and these mutations eventually cause cancer in the body due to incorrect transcription of proteins. All cells in the body are endangered because of radiation, and there are many short- and long-term health consequences.

2. Hydrogenous materials [4]

Dihydrogen (H2) is an excellent radioprotective substance that shields against ionizing radiation that causes apoptosis of cells. This can help protect astronauts from the harmful effects of radiation during space travel. Ionizing radiation can break chemical bonds and strip electrons from atoms and molecules, causing serious damage such as cell death. Dihydrogen (H2) can protect against cell death caused by radiation, which is essential for the health and safety of astronauts during space travel. In conclusion, the radioprotective properties of dihydrogen (H2) can be useful in space suit design. By shielding against ionizing radiation, protecting against cell death, and potentially acting as an antioxidant, dihydrogen (H2) can help protect astronauts from the harmful effects of radiation during space travel.

3. Melanized Fungi [5]

Melanin, the pigment of skin, has many radioprotective properties that can be applied to space exploration. On Earth, some environments have high background radiation, such as the remains of Chernobyl. Even still, animals can survive and adapt to their new surroundings. Melanized fungi are more common in Chernobyl areas, and studies
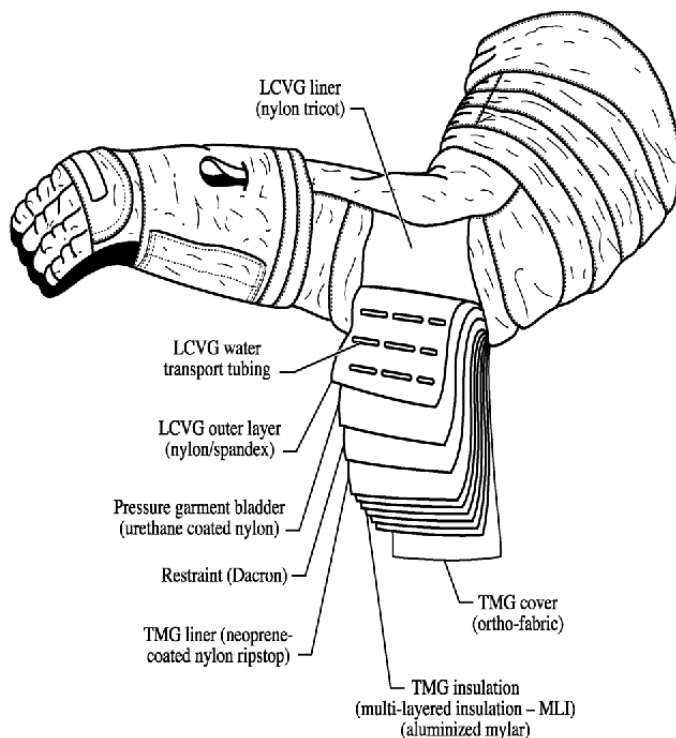
reveal that non-melanized fungi can have the protective effects of melanin transferred to their cells. Melanin is a possible substitute for the several layers of current space suits that protect against radiation.

Thermoregulation

1. Fur

On Earth, there are several environments with subzero temperatures. Although these temperatures are daunting, several animals have adapted and now inhabit these areas. Fur is a natural insulator that animals use. When insulation is high, heat transfer is low. Seals and whales also have a thick layer of blubber for insulation. Different parts of the body require different amounts of insulation. Thus, the amount of blubber can vary from the region of the body, which assists in movement.

2. Heat reflection (SWME)[6]

The human body cannot survive the harsh conditions of space and requires the assistance of technology to maintain comfortable conditions. Circulating water around the space suit allows it to absorb excess heat. The warm water is
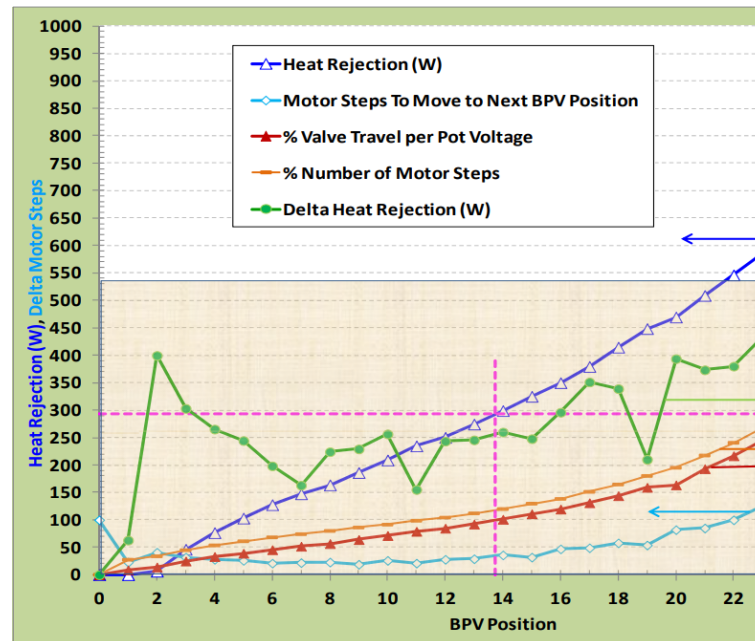
filtered through the SWME, where it is evaporated and recirculated. Furthermore, the SWME also prevents circulated water leakage, drastically improving astronaut safety. Although the SWME is highly experimental, it is a powerful way to maintain cool temperatures in space.

Figure 2: Heat Absorption from SWME. Increased water movement proportional to heat rejection

3. Thermal emitters [7]

Morpho butterflies have a distinct blue color that could be applied to achieve radiative cooling in space suits. The structure in the image below represents the pigmentation in the butterflies that can be integrated into space suits to decrease heat further.

Maneuverability

1. Boots[8]

Space suit boots cause significant problems when attempting extravehicular activities in space. Current space suits are not conducive to the advancement of science as scientists are almost always looking at the ground to ensure that they do not fall over anything. This is due to the number of layers astronauts must wear, resulting in their inability to feel the ground below them.

2. Custom space suits[9][10]

Current space suits are also highly oversized for the astronauts who wear them. Suppose custom space suits were created for each astronaut. Using new digital thread technology, astronauts can move like usual, as if on Earth. A small, stretchy, skin-like suit would be perfect for this type of technology, as digital thread technology could easily map out how tight the suit must be.

Debris protection

1. Spider Silk[11]

Spider silk is a robust material that could be applied in micrometeoroid protection. Spider silk is extremely durable due to the long strands of protein that compose it. Spider silk also comes in many variations. Some are strong and protective, while others are conducive to movement and flexibility. Spider silk is also easy to mass produce as genetically engineered goats make them along with their milk.

2. Kevlar[12]

Current debris protection technology in space suits mainly consists of kevlar padding around the suit to prevent injury to the astronaut and the technology in the suit. Kevlar also protects against leakages in the suit and helps to retain heat. Although Kevlar is highly versatile, it struggles against compressive strength and restricts astronaut movement.
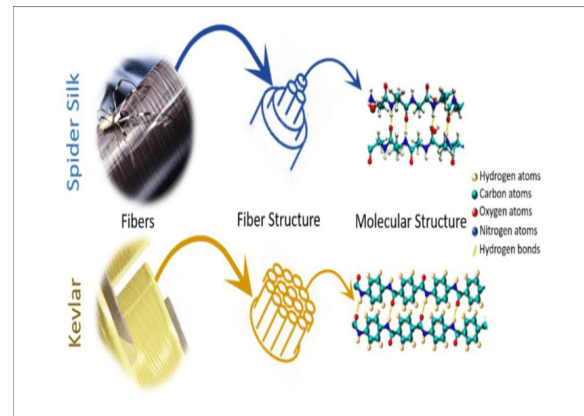
Conclusion

Utilizing biomimetic design principles for modern space suits may yield several advantages. Biomimetic designs provide astronauts with enhanced safety during spacewalks and other activities by mimicking plant and animal features for added protection from radiation, debris, and other threats in space. Spacesuits with biomimetic designs offer greater protection during these activities by mimicking protective features found on plants and animals that help ensure astronauts' well-being in space.

Biomimetic designs also help increase the mobility of space suits by mimicking animal movements and flexibility to enable astronauts to perform tasks more easily and quickly. By mimicking animal mobility and dexterity in design, spacesuits provide astronauts with a greater range of motion and dexterity.

Better Thermoregulation: Space suits designed with biomimetic designs can assist astronauts with maintaining optimal temperatures inside space suits, providing more precise temperature regulation during extreme temperatures. By mimicking animal fur or feather insulation properties, these suits may offer enhanced temperature management for astronauts.

Biomimetic designs can also make space suits more durable and easier to maintain by mimicking certain self-repairing features found in certain plants and animals; spacesuits designed using biomimetic designs will better stand up against space's harsh conditions, with fewer maintenance requirements over time.

Our understanding and ability to utilize space depends on improving space suits, specifically how we can use nature to our advantage with biomimetics. Although current space suits are functional, many aspects can be improved upon. Radiation protection, thermoregulation, enhanced mobility, and debris protection are only a few of the improvements that biomimetics can bring to the space industry to improve the lives of astronauts.

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