NOVACRYPT

NEWSLETTER

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Upcoming Dates:

Oct 8: Summer Program Winners Announced

Oct 8: Fall Topic Announced

Oct 9: Competition Cycle Officially Begins

Nov 24: All Competition Material Due

Dec 1: Look for the next issue of our newsletter for winners and information about December activities and our January-February competition cycle!

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Welcome to NovaCrypt!

You may have heard of us through social media, research projects, or school, so let us take a moment to introduce ourselves! We are NovaCrypt, a 501c(3) nonprofit dedicated to bringing STEM education and opportunities across the United States, and eventually the world. We host a number of competitions and programs designed to get high school students involved in research, promote STEM education with real world applications, and foster a community of future professionals.

Not interested in STEM? Our approach allows you to tackle our topics from whatever lens you can see. Interested in law? Tell us the legal implications of AI or space policy. Interested in business or finance? How can space exploration further economic opportunities, or how can deep see research benefit society outside of obtaining knowledge. Solving big problems requires collaboration across disciplines.

For those interested in pursuing a career within the STEM focused fields, our programs will allow you to build up your resume with research, mentoring opportunities and more! You can explore whatever you are passionate about, from coding, to physics, to biology. Our topics are designed to be approached from as many different disciplines as possible, and there are always points for creativity!

Outside of our chapter based competitions, look for leadership building opportunities on our staff, educational opportunities, workshops, mentorship, and more! We are always working to improve what we can offer. Participating in NovaCrypt is a great way to gain experience, awards, connections, and opportunities.

We cannot wait to see all you will achieve this year, and wish you the best of luck in all your endeavors both with us and throughout your educational journey!

NIT Sikkim Initiative Wrap-Up:

In the summer of 2023, Novacrypt and the National Institute of Technology, Sikkim (NIT Sikkim), partnered and focused on nurturing student enrichment in project development. Over six weeks of this collaboration, students could pursue their passions and create innovative solutions. With 24/7 stand-by help and guidance, we are very happy to conclude a successful internship.

This initiative allowed students to select projects aligned with their interests, resulting in diverse projects. Some notable projects included an AI-powered healthcare assistant, an eco-friendly waste management system generating renewable energy, an emotion detector, and even a social media app!

As Novacrypt and NIT Sikkim look ahead, we are eager to expand this initiative, inspiring even more students to drive innovation and shape the future. This partnership shows us the power of passionate, guided learning and highlights the potential of the next generation of innovators. Stay tuned for more groundbreaking projects to come!

All you need to know about our Chapters:

So, you want to form a chapter? Great! Here's how!

NovaCrypt Chapters are the primary focus of our STEM outreach, and easy to start! All you need are some students and a faculty advisor, and you can get started competing against schools all over the nation!

But what is a chapter? A chapter is run like a club, where you have your individual group within your school, your own officer team, and an advisor who communicates with NovaCrypt at a national level. Club officers will include a President, Vice President, Secretary, Treasurer, and Historian. These duties are outlined in the Club Constitution, which will be sent out upon registration. This gives lots of leadership opportunity at the Chapter level.

Competitions will be held in cycles. The fall cycle will be from Oct. 9-Nov. 24 when all competition material is due. The projects will then be judged and results published in early December. The next cycle will be announced for January-February and April-March, which will conclude the regular competition cycle. Each cycle, a prompt will be announced in our newsletter, as will the winners.

So how do you compete? Chapters are encouraged to meet once a week, especially during competition cycles. Once your chapter sees the prompt, the first week should involve sitting down as a chapter and looking at possible "lenses" or approaches. We will always provide some examples, but those are never the only possibilities. The chapter should then divide into groups of 1-5 students per lens you with to pursue. For example, 3 members of your chapter may wish to pursue a topic from a biology lens, 2 with computer science, 1 with physics, and so on. Lenses will be competing against others who select a similar lens, so you would not be competing against your own chapter by selecting different lenses!

Winners will be selected in categories by lens, which also means you could win based on creativity and finding an approach no one else has thought of! The winners of each

lens will be announced, as well as an overall Grand Champion and special awards.

Your advisor will be responsible for turning in all competition materials. The final product will be you and your group addressing the prompt in both a written and video format. Rubrics for both will be available and sent to your advisors. You may chose to respond by proposing an initiative and writing a project proposal, submitting a research paper, or providing an example of your proposed solution. Then your group will record a video explaining your project and submit all materials before the deadline.

This is a great chance to grow your skills, compete at a national level, and collaborate on great projects with modern applications. Students will not only win our competitions, but have the potential to be recognized by many of our professional mentors, receive individual support, participate in workshops, and gain valuable insight from college students, professors, and professionals.

Your Fall Topic:

The topic chosen for the first round of the 2023-2024 school year is “Human Augmentation: Risk Versus Reward.” NovaCrypt chapters will be embarking on an exciting exploration of Human Augmentation. As technology and science continue to push the boundaries of what's possible, our relationship with augmentation evolves, presenting both unparalleled opportunities and ethical dilemmas. Students are encouraged to do research on this topic through a number of lenses and form their own conclusions. Projects submitted should be formatted as a research paper, project proposal, or a written example and be accompanied by a video. Please see rubrics and later releases for more information! Get started as soon as you can on deciding your lenses and beginning your projects. All material is due on November 24th, 2023!

Suggested Approaches:

Computer Science: Dive into the realm of wearables and augmented reality. How are these tools shaping our perception and interaction with the world?

Engineering: Understand the mechanics and innovations behind augmentation technologies. What makes them feasible, and where are the technological limits?

Business: Examine the market trends surrounding enhancement products. What's the demand, and where is the industry headed?

Biology: From prosthetics to genetic engineering and biohacking, discover the cutting-edge developments that are redefining human potential.

Politics: Delve into the ethical implications and regulations of human enhancement. How do we strike a balance between innovation and morality?

How to Sign Up:

Use the form in our discord or Instagram Linktree to register your chapter. You must include your faculty advisor’s email, as all communication will be sent to them. You will be eligible to compete up to the last day of the cycle, but the earlier you register, the more material and support you will receive from our staff and judges!

Remember:

You may approach the prompt from whatever discipline you want! If your interest isn’t listed, we challenge you to be creative and pursue whatever you are passionate about!

Summer Program Summary

The NovaCrypt Summer initiative gave high school students a chance to work with undergraduate mentors on a research project of their choice. With mentor guidance, these students prepared a research paper which was then ranked by a panel of undergraduates, graduates, and professors that were not involved in the mentorship process. These papers were judged on the given rubric, quality of content, and overall report. Students were also asked to create a poster to better understand how researchers present their work, and to record video presentations. The posters were not counted during ranking, but they were used as tiebreakers. Videos can be found on our YouTube page!

Meet our Winners:

First Place:

Alyssa Molock
Sussex Technical High School
Georgetown, DE

Second Place:

Mackenzie Lopez
Pope Francis Preparatory School
Springfield, MA

Third Place:

Victoria Wroblewski
Commack High School
Commack, NY

Fourth Place:

Anika Krishnan
Irvington High School
Fremont, CA

Fifth Place:

Audrey Ng
Portola High School
Irvine, CA

Special Thanks:

Thank you to all the students who competed! Our program was able to support 50 students, and congratulations to our top 5 winners!

NovaCrypt would like to offer a special thank you to our undergraduate mentors who helped the participants with their projects:

- Jenna Bahnken
- Avanish Davuluri
- Youssef El Gharably
- Alaena Mackenzie
- Adam Jameel
- Bri Johnson
- Jowaii Soetamin

**Note: Some papers have been altered from their original format in order to keep the newsletter a reasonable length. ABSOLUTELY NO CONTENT has been altered in any way, and the work remains that of the participants. NovaCrypt is not responsible for any accidental copyright infringement on the part of the students due to improper citation and is not responsible for validating the facts and research presented.

Neurological Insights into Generalized Anxiety Disorder: Exploring the Vital Roles of the Amygdala and GABA

Alyssa Molock

Class of 2024, Sussex Technical High School, Georgetown, Delaware

August 19th, 2023

Abstract

Generalized Anxiety Disorder (GAD) is a disorder that has affected individuals worldwide for centuries. Though it falls under the umbrella of Anxiety Disorders, GAD patients have symptoms that affect them differently than any other anxiety disorder. This research paper investigates the neurobiological mechanisms that make up GAD. Findings below have a specific focus on the roles of the Amygdala and GABA levels. Through a comprehensive review of existing studies and literature, the research shows positive connotations between an overactive Amygdala and low levels of GABA in the brain. The goal of this study is to dig deeper into the neurochemical basis of GAD, in hopes to develop medications to prevent this disease or to assist the already affected patient.

Generalized Anxiety Disorder, Defined

Generalized Anxiety Disorder (GAD) is a psychiatric disorder characterized by excessive and persistent feelings of worry and dread about many daily activities—that of which negatively interferes with the individual's everyday function. GAD is identified with psychological symptoms consisting of restlessness, fatigue and irritability along with physical symptoms of muscle tension and headaches. (Mayo Clinic, 2017) Many believe the etiology of the disease may include, stress, genetic factors and environment-based disruptions in the individual's lives. Findings that that at around 4% of the global population, around 301 million people suffer from an anxiety disorder worldwide, (Javaid et al., 2023) though not all are GAD-related. Risk factors include being female, low socioeconomic status and childhood adversity. (Madonna et al., 2019) Though there is no cure for GAD, it is a treatable illness, commonly managed with prescribed medicines and therapeutic inventions.

Because it is an uncurable disorder, it is inferred that quality of life for these patients is considerably lower than those unaffected. A major complication for those who have GAD is depression. Studies show that depression is a common result for those who have been diagnosed with Anxiety. In a research article describing the relationship between Anxiety and depression posted on the American Journal of Psychiatry, Ned. H. Kalin, MD., comments that Anxiety and depression are "comorbid" with each other. Additionally, in his study, Kalin found that 43% of patients with Generalized Anxiety Disorder were diagnosed with depression. (Kalin, 2020) Additionally, insomnia, social isolation, and suicide potential are considerable complications for GAD patients. (Munir & Takov, 2022)

Many scientists believe the disorder arises from hyper-reactivity in the Amygdala. The Amygdala is the part of the brain that process the body's emotions, including fear. (C.C Medical) When the amygdala is hyper-reactive, the human might face a higher risk of going in "fight or flight" mode, resulting in a constant state of fear or worry. Also, low levels of the neurotransmitter Gamma-aminobutyric acid (GABA), may also be the cause. The following research describes the brain function of patients with Generalized Anxiety Disorder and demonstrates the neurological differences between GAD Patients and those unaffected, while focusing on the roles of the Amygdala and GABA in the brain.

History / Background

Austrian Neurologist Sigmund Freud was the first person to recognize Anxiety as the disorder it is now. The physician coined the term “anxiety neurosis” in 1895, when he came up with the etiological theory of the phenomenon. His second symptom the “anxious expectation” is a key symptom in what Generalized Anxiety Disorder is today. (Crocq, 2017) Freud listed an example “A woman, for instance, who suffers from anxious expectation will think of influenza pneumonia every time her husband coughs when he has a cold, and, in her mind's eye, will see his funeral go past.” Essentially, visualizing the situation of fear and worry in a situation similar to his at the time. That women’s reaction was Freud’s version of modern-day Anxiety. Centuries later, the term Anxiety, as a whole, has changed drastically in history.

In 1980, when the American Psychiatric Association published the Diagnostic and Statistical Manual of Mental Disorders (DSM-III), GAD was first introduced. Then, it had been described as “Generalized, persistent anxiety”. In the DSM-5, it had been described as “Excessive anxiety and worry [apprehensive expectation] about a number of events or activities. Difficult to control the worry.” (Crocq, 2017) Prior to this, in DSM-1, Anxiety was mentioned in a chapter titled “psychoneurotic disorders”, where anxiety was seen to be a danger signal which was produced by a threat from within the person. The ‘anxiety reaction” was seen to be the reaction to said danger signals; though the reactions were differentiated from normal apprehensiveness or fear. In DSM-II, the reaction of DSM-I had been renamed “neuroses”, then characterizing the term “anxiety neurosis” as anxious over-concern extending to panic and frequently associated with somatic symptoms. Which then became the precursor to the Generalized Anxiety Disorder commonly known to psychiatrists in modern times. (Crocq, 2017)

As noted before with Dr. Kalin’s study, when the DSM-III defined Generalized Anxiety disorder, many commentators acknowledged the comorbidity of GAD and depression. Because of this, some suggested the disorder should be “conceptualized as a prodrome, residual, or severity marker than as an independent disorder.” Though, as research went on, data showed that “generalized anxiety disorder is a common disorder that, although often comorbid with other mental disorders, does not have a higher comorbidity rate than those found in most other anxiety or mood disorders.” (Munir & Takov, 2022).

The Causes

As the Amygdala activates the “fight-or-flight” response within the individual, for GAD patients, this means they are constantly on high alert. Anxiety is rooted within the stress hormones the hyperactive Amygdala sends the body. With these responses, the body responds with fear-actions including an increased heartbeat, tense muscles and heavier breathing. For Generalized Anxiety Disorder patients, there does not need there to be a stressor for them to experience these symptoms. It is common for patients to have no specific reason for their actions. (Harvard Health, 2014) Additionally, in a study found with the Stanford School of Medicine, research has shown that the amygdala regions in GAD patients had less connectivity to the brain responsible for determining the importance of stimuli. (Pappas, 2009). From this, patients have demonstrated their inability to discern the level of concern with situations they are put in.

Gamma-aminobutyric acid (GABA) is the chief inhibitory neurotransmitter in the nervous system. It is a chemical messenger that sends signals to the brain. The purpose of GABA is to reduce neuronal excitability by inhibiting nerve transmission, in result decreasing the level of neuronal stimulation in the brain. (Allen et al., 2023), However, low levels of GABA have been shown to be linked to GAD. Research provides proof that decreased levels of GABA can lead to a feeling of anxiousness with individuals who have abnormalities in the neuro-transmitter.

Some studies demonstrate low levels of GABA could be a part of the GAD patient’s genetics—however, genetics in relevance to GAD are seen to be less substantial than other anxiety disorders.

Though studies have proved that first-degree relatives of family members who have GAD have higher rates of mood and anxiety disorders in general, scientists have presumed it to be the same with an increased risk of the disease in general. Findings in brain scans for pediatric patients with GAD demonstrate high rations of gray matter to white matter in the temporal lobe. (Martin et al., 2023) This study suggests the pediatric subjects have been subjected to stress-induced amygdala hypertrophy after prolonged exposure to the illness. Additionally, in a finding with adolescent GAD patients compared to healthy subjects, GAD patients have found resting activity in the ventrolateral prefrontal cortex (vlPFC) to be elevated compared to healthy subjects. This is presumed to be a compensatory response to the disease. (Madonna et al., 2019)

Demographics Affected

However, it should be noted that brain imaging scans between GAD patients tend to be inconsistent—leading to the conclusion that the disease affects each person differently. Females tend to be affected with Generalized Anxiety Disorder as compared to men. Regarding age, in a study concluded debating the age of GAD patients and how it affects them, results led to younger-middle aged adults showing more symptoms of anxiety, worry, negative affect and depression while compared to older adults. In addition, younger adults experienced fewer somatic anxiety symptoms, but higher worry and negative affect than middle-aged adults. Additionally, tending to race, African-Americans were found to be less likely to be taking medications and seeing mental health providers as compared to their white counterparts in the study. (Brenes et al., 2008)

There are many theories that GAD can affect people based on their race, genetics, age, etc., but there needs to be more studies before the conclusion can be drawn. With the help of neuroimaging and additional data, only then can scientists find the link to who is most likely to be affected by this disorder.

Common Medications

Medications are commonly prescribed to patients suffering from Anxiety disorders. Selective serotonin reuptake inhibitors (SSRIs) and Serotonin-norepinephrine reuptake inhibitors (SNRIs) are, generally, Doctor's first choice medication for GAD patients. They consist of drugs such as Citalopram, Fluoxetine and Paroxetine, all medications that increase levels of serotonin in the brain. Drugs such as these are preferred as they have 'broad spectrum' efficacy in both short-term and long-term treatment, and are generally well tolerated; and for these reasons, the British Association for Psychopharmacology stated that SSRI's "are widely considered to be the first-line pharmacological approach in patients with anxiety disorders" (Strawn et al., 2018) Though, some SSRIs are at risk of withdrawal symptoms at the end of treatment.

If not prescribed with SSRIs, a second choice medicine is Benzodiazepines. Studies show that 55 to 94% of anxiety patients have been treated with benzodiazepines. This medicine is used as a depressant, which provides sedation and can reduce anxiety within the patients. In the patient, Benzodiazepines tell the brain to release GABA neurotransmitter signals, in attempt for the nervous system to have slowed activity. This is ideal for GAD patients as benzodiazepines do not lead to increased jitteriness or insomnia. Though, there are negatives to the medication. It can lead to CNS depression—fatigue, dizziness and impaired driving skills are a few negatives. Additionally, after prolonged use, the patient might get dependent on the drug. The withdrawal symptoms are much more adverse than withdrawal symptoms to an SSRI.

Phytotherapy, the use of plants or herbs as a medication has shown positive results in many studies. There are theories that a lavender pill could be used as a medication to GAD, however there have been inconsistent results to the study. (Bandelow et al., 2017) For older patients, there are risks of sensitivity to the medications as they have higher fall risks and risks of cardiovascular events.

Antipsychotics and Buspirone are also medicated choices for patients.

For those who choose to not take medication for their diagnosis, Cognitive Behavior Therapy (CBT) is a choice. Some examples of CBT include psychoeducation, changing maladaptive thought patterns, and gradual exposure to anxiety-provoking situations. (Munir & Takov, 2022). CBT is a way for GAD patients to be in touch with their feelings towards the disorder so they can work out and analyze their thoughts, feelings and behavior patterns towards themselves and their diagnosis.

Possible Solutions

Additional emerging research shows that scientists have been doing studies regarding serotonin, melatonin and neuropeptides in the brain in an attempt to find more medications to fight anxiety-related diseases (Murrough et al., 2018), medications that work positively similar to SSRI's and SNRI's.

Additionally, natural remedies utilizing the Kava plant have been considered. It contains kavapyrones, which many think can "exert anxiolytic effects through activity on sodium and calcium channels or most likely from action on GABA-A receptors (like benzodiazepines)" Findings support that there were reductions in anxiety, however it was noted Kava could be recommended for short-term use, though is not recommended to replace long-term medications. Scientists have noted severe liver toxicity when using kava. Several other natural remedies include ashwagandha, passionflower, echinacea, ginkgo, chamomile, lemon balm and valerian, though none show as much promise as the kava plant. (Garakani et al., 2020)

It should be noted that there are not many studies that are finding positive results when it comes to treatment for Generalized Anxiety Disorder.

Final Remarks – Summarizing the Findings

Research and findings are constantly being done in attempt to find more medications and learn more about the disorder known as Generalized Anxiety Disorder, though there are theories, there is always more to know about the brain. Some key takeaways in my research highlight that the cause of GAD is from a hyperactive amygdala, which then provides the fight-or-flight actions in the body and possibly an abnormally low level of GABA in the patient's brain, which leads to the symptoms of a constant state of fear with the GAD patient. Findings cannot conclude that there are patterns concerning genetics or demographics for affected patients. These are highly supported claims, though more research is being done to treat and find the cause of this disorder in the patients.

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Exploring Innovative Approaches for Advancing the 3 R's in Research: Moving Beyond Animal Testing through Biological, Biochemical, Ethical, and Multi-Cellular Strategies – Can We Eliminate the Need for Animal Testing?

Nova Crypt Summer Research Mentorship Program (Virtual)

Mackenzie Lopes – Mentored by Youssef El Gharably

2024, Pope Francis Preparatory School, Springfield, MA

Abstract

With the further development of medical technology research and development, the number of animals used in research is increasing. Every year, millions of laboratory animals are used around the world. The pain, suffering, and death of animals during scientific experiments have long been a controversial issue. In addition to major ethical concerns, animal experiments also have several drawbacks, such as the need for qualified personnel, time-consuming protocols, and high costs. A 3R strategy (i.e., reduce, purify, substitute) is employed for the use of animals in laboratories. Various methods and alternative organisms are used to carry out this strategy. These methods are alternatives to drug and chemical testing in specific fields, and this review describes and provides examples of these alternatives and their associated advantages. Integrated application of these approaches will minimize the use of animals in scientific experiments.

I. Introduction

The use of animals for various purposes, such as food, transportation, pets, sports, recreation, and society, is as old as humans, and the use of animals in research is one of its extended uses. Various animals such as mice, rats, hamsters, rabbits, fish (e.g. zebrafish, trout), birds (mainly chickens), guinea pigs, amphibians (Xenopus laevis), primates, dogs and cats have been used in research for many years (CULABBR, 1988). The primary goal of such studies is to conduct drug testing and toxicity screening to aid in the development of new treatments for infectious and non-communicable diseases. Animals also serve as tools for making sense of medical procedures and surgical experiments. In addition, it is used to obtain vaccines, antibiotics and other products that are used both diagnostically and therapeutically (Giacomotto and Segalat, 2010; Hendriksen, 2009, 2007). With the further development of medical technology, the number of animals used in research has also increased. Every year, millions of laboratory animals are used around the world. For example, in the UK, 3.71 million animals were used in research in 2011 (www.rspca.org.uk). The total number of animals used was estimated at 1,131,076 he in the United States in 2009, while in Germany it reached a maximum of 2.13 million in 2001 (Rusche, 2003). This large experimental animal population typically comes from various university breeding centers and national breeding centers. These are all referred to as Class A dealers, while intermediaries who obtain animals from various sources (such as auctions and animal shelters) are referred to as Class B dealers. In some cases, wild animals such as monkeys and birds are also used (Baumans, 2005). In clinical laboratories, animals are isolated from their group and used as tools regardless of their natural instincts. Whole animals or their organs and tissues are used in experimental procedures. For this purpose, animals are euthanized (slaughtered) according to established methods. Animals that survive clinical trials are often euthanized at the end of the experiment to avoid subsequent pain and suffering (Rusche, 2003). In some cases (e.g. LD 50 analysis), animals die as a result of experiments.

The pain, suffering, and death of animals during scientific experiments has long been a controversial issue. The argument is that if animals are alive, they have the right to alleviate pain and suffering, and

therefore the use of animals in experiments is unethical and should be stopped (Rollin, 2003). Various laws and regulations have been enacted to regulate the unethical use of animals and to minimize animal suffering during experiments. For example, animal rights organizations were founded in 1824 by the Royal Society for the Prevention of Cruelty to Animals. In 1876 Britain passed a law to prevent cruelty to animals (Balls, 1994). Founded in 1960, 1963, and 1966 in India, Franc,e and the United States. Many rules and laws are now followed internationally to protect animals from cruelty and cruelty. Besides major ethical concerns, animal experiments also have drawbacks, such as the need for qualified and trained personnel and time-consuming protocols. Furthermore, the very high cost of breeding, rearing, and lengthy animal testing protocols is another drawback. (Balls, 1994).

II. Three Rs: reduction, refinement, and replacement

Alternatives to animal testing have been developed to address some of the difficulties of animal testing while also avoiding unethical activities. The 3R strategy is applied. This means reducing, improving, or replacing the use of animals in laboratories (Ranganatha and Kuppast, 2012). Various methods and alternative organisms are used to carry out this strategy. The concept of animal substitution was first discussed by Charles Hume and William Russell at the Union of Universities for Animal Welfare (UFAW) in 1957 (Balls, 1994). Russell and Burch (1959) proposed several ways of humanizing animal experiments, later called the 3Rs. This approach motivates the use of minimal numbers of animals. H. "Reduction" in the total number of animals used in the experiment. Animal use must be carefully planned and 'refined' to minimize pain and distress during the experiment. Animal substitution is defined as "any scientific method of using non-sensory substances that can replace the use of conscious living vertebrate animals in animal experiments". He distinguished two kinds of substitutions, ``relative" and ``absolute". Animals are used as relative surrogates but are not subjected to stress during the experiment. Withdrawal of the animal at any point in the experiment has been identified as an absolute alternative strategy (Balls, 1994).

2.1. Reduction

Experiments can produce relevant scientific results with the use of statistical support and appropriate research design. For example, in vitro cell culture is a good way to test compounds in the early stages. Human hepatocyte cultures provide information about how drugs are metabolized and cleared from the body. Incorporating such methods into the research plan can help preempt inappropriate compounds and minimize the use of animals in further testing (Kimber et al., 2001). The effects of some compounds on embryonic development have been studied in live animals and embryos. In vitro studies using embryonic stem cell cultures help reduce the number of live embryos used and the number of compounds toxic to developing embryos (Gipson and Sugrue, 1994; De Silva et al., 1996). Additionally, the transferability or availability of the data obtained (e.g. excipient properties of the study drug) avoids the need for animal testing.

2.2. Refinement

Reduce animal stress by enriching the cage environment through animal care. Scientists need to improve animal husbandry practices to reduce pain, discomfort and stress during animal life and scientific procedures. Additionally, any stress or discomfort can create an imbalance in the animal's hormone levels, which leads to variability in results. Therefore, it is necessary to repeat the experiment, and the number of experimental animals increases. For example, when mice genetically engineered to study HD were given a complex cage environment with the ability to nest, hide, gnaw and feed, they observed that the disease progressed more slowly than mice housed in sterile cages. It was also found that such mice mimic the
human disease course better. Such improvements provide a very good model for treating disease and also minimize stress on animals (De Silva et al., 1996). 2.3.

2.3. Replacement

Various alternatives to the use of animals have been proposed, including in vitro models, cell cultures, computer models and new imaging/analytical techniques (Balls, 2002). In vitro models offer the opportunity to study cellular responses in a closed system where experimental conditions are maintained. Such models provide preliminary information about the outcome of in vivo experiments. For example,

computer models have been used to study cardiac function and select potential drug candidates (Gipson and Sugrue, 1994). In many countries, in vitro cell cultures have replaced skin irritation and Draize eye irritation tests, as well as the use of animals. Another example is the extraction of insulin from porcine or bovine pancreas, now extracted from bacterial cultures, making it an essential medicine for diabetics. This extracted insulin must be checked for purity, potency and dosage. Animals were routinely used for such checks, but chromatographic techniques are now used to check purity, potency, and drug dosage calculations (Foreman et al., 1996). Overall, the alternatives significantly reduce the use of animals in various processes.

III. Alternative methods

Various methods have been proposed to avoid the use of animals in experiments. These methods offer an alternative to drug and chemical testing in specific areas, with the benefits of time efficiency, personnel reduction, and cost efficiency. Details of these methods are as follows:

III.1 Computer Models

Computers help us understand many basic principles of biology. Special computer models and software programs help develop new drugs. Computer-generated simulations are used to predict various potential biological and toxic effects of chemicals or potential drug candidates without the need for animal dissection. Only the most promising molecules from the primary screen are used for in vivo experiments. For example, in vivo experiments are required to know the receptor binding site of a drug. A software called Computer Aided Drug Design (CADD) is used to predict receptor binding sites for potential drug molecules. CADD identifies potential binding sites and avoids testing for unnecessary chemicals that have no biological activity. Furthermore, with the help of such software programs, new drugs can be tailored to specific binding sites and subjected to final-stage animal studies to obtain confirmatory results (Vedani, 1991). This reduces the total number of experimental animals and fulfills Russell and Birch's 3R goal.

Another popular tool is the structure-activity relationship (SAR) computer program. Predict biological activity of drug candidates based on the presence of chemical moieties attached to the parent compound. A quantitative structure-activity relationship (QSAR) is a mathematical description of the relationship between the physicochemical properties of a drug molecule and its biological activity (Knight et al.,
2006). His QSAR software now provides better results while predicting the carcinogenicity of each molecule. Speed and relatively low-cost procedures are two benefits of computer models over conventional animal models (Matthews and Contrera, 1998). A very good example is the study by Dewhurst et al. (1994) investigated the effectiveness of computer models compared to conventional laboratory practice. In this comparative study, two groups of students conducted experiments using traditional wet lab approaches and computer-assisted learning (CAL), respectively. CAL is an interactive computer-aided learning (CAL) program that does not require real lab tools. At the end of the study, both groups' knowledge acquisition was assessed (through test questionnaires, calculations and interpretations).

III.2 Cells and tissue cultures

The use of in vitro cell and tissue culture to grow cells outside the body in a laboratory setting can provide an important alternative to animal testing. Cells and tissues, such as liver, kidney, brain, and skin, are harvested from animals and can be stored in vitro in an appropriate growth medium for days, months, or even years. In vitro culture of animal/human cells separates the cells from each other and grows as a monolayer on the surface of culture plates/flasks. Cellular components such as membrane fragments and cellular enzymes can also be used. Different types of culture are used depending on the purpose, such as cell culture, callus culture, tissue culture, and organ culture. The advantages associated with this technique are that it is easy to follow, quick and inexpensive. These methods are routinely used for preliminary screening to assess the toxicity and efficacy of potential drug molecules/chemicals (Shay and Wright, 2000; Steinhoff et al., 2000). These tests test the toxicity and efficacy of nearly all cosmetics, pharmaceuticals, and chemicals. For example, eye irritation test. In the past, the Draize test, which requires animals (mainly rabbits), was used to confirm the irritant potential of chemicals. “Every time I

use a new animal it is very painful" (Ke Ping Xu et al.), proposed an alternative using bovine corneal organ cultures. Bovine corneas are cultured in the laboratory for up to 3 weeks, and various analytical methods are used to assess the toxic effects of the irritating effects of test chemicals in vitro (Xu et al., 2000).

III.3 Stem cell research:

As a complementary option to using animals for toxicological studies and disease modeling in vitro, stem cells may be useful. Disease genes are inserted into embryonic stem cells, which are then induced to differentiate into human disease tissue that can be used for drug screening. ES cells proliferate in petri dishes and differentiate into various cells that make up human organs. These in vitro versions of human tissues are superior to single-cell type shells when evaluating the toxicological effects of drugs. These provide a human impact profile, not a mouse impact profile. Researchers used genes from Parkinson's disease patients to create embryonic stem cell lines that exhibit degenerative manifestations of the disease. Diabetes and Alzheimer's disease have been found to be associated with a combination of genetic and environmental causes, and stem cells are being used to test new drugs to treat these common diseases. Embryonic stem cell-derived mouse models of two spinal cord disorders, spinal muscular atrophy and Lou Gehrig's disease, have been developed to test new drugs.

Mammals are not always good models, especially when it comes to delineating a drug's potential hepatotoxicity and cardiotoxicity. Animal models are expensive and time-consuming to obtain results. Stem cells offer a better alternative material for studying various types of cancer, as well as liver and heart toxicity.

III.I Results - Alternative Organisms

Ethical concerns impose many restrictions on the experimental use of higher model vertebrates such as guinea pigs, rats, dogs, and monkeys. Therefore, the use of alternative organisms has been proposed. Various model organisms are used as an alternative to experimental animals (Table 1).

Table I: Selected Examples of Organisms

Alternative Organism (s)	Specific Cellular Function
Escherichia coli	**Model for molecular/genetic studies (prokaryote)**
Bacillus subtilis	**Model for cellular differentiation (prokaryote)**
Saccharomyces cerevisiae	**Model for gene expression (cell cycle, fungi)**
Genus ascomycetes	**Model for population genetics (fungi)**
Aspergillus nidulans	**Model for genetic / cell biology (fungi)**

3.3.2.2. Example – Caenorhabditis elegans

Caenorhabditis elegans is a eukaryotic nematode. This multicellular organism is about 1 mm long and has a very short generation time. The entire life cycle of this hermaphrodite is about 2-3 weeks. Embryogenesis occurs in 12 hours and adults develop in 2.5 days. It is transparent, genetically accessible, and exhibits simple cellular complexity. It was therefore chosen as a model organism by Nobel laureate Brenner (Barr, 2003; Strange, 2007). The C. elegans life cycle progresses through various complex developmental stages, including embryogenesis, morphogenesis, and adult development. This is he one of the most commonly used model organisms for research purposes. The information obtained may also be applicable to more complex organisms such as humans. C. elegans is used as a model to study various neurological diseases such as Huntington's disease, Parkinson's disease, and Alzheimer's disease. Various immune diseases, cancer, diabetes, etc.

3.3.3. Microorganisms

3.3.3.1. Example – Saccharomyces cerevisiae

The brewer's yeast Saccharomyces cerevisiae is the most popular and important model organism due to its rapid growth, ease of replication plating and isolation of mutants, dispersed cells, well-defined genetic system, and highly versatile DNA transformation system. Yeast can be grown in solid or liquid culture and isolated as colonies derived from single cells on solid media. The very short generation time of about 90 minutes makes breeding and analysis of large populations very easy (Mell and Burgess, 2002). The entire genome of this unicellular fungus was sequenced in 1996. The nuclear genome contains approximately 16 chromosomes with over 13 million base pairs. Mitochondria also contain an additional nuclear genome. Reproductive yeast carries genetic information in the form of 6000 genes. The number and size of genes are relatively small and the gene density is very high. S. cerveisiae is one of the most well-characterized and studied genomes, making it one of the most ideal eukaryotic microorganisms for biological research. Having a similar cellular structure and basic life cycle to multicellular eukaryotes is another advantage. Numerous membrane-bound organelles such as the nucleus, peroxisomes, mitochondria and secretory pathway organelles also mimic mammalian cell function (Mell and Burgess, 2002). This brewer's yeast has been used to understand human programmed cell death and cell death regulators, and is very useful for cancer research (Madeo et al., 2002). By studying the endogenous or heterologous proteins that underlie neurodegenerative diseases such as Alzheimer's, Parkinson's and Huntington's diseases, S. cerevisiae helps us understand fundamental aspects of cell biology in these diseases (Pereira et al., 2012; Siggers and Lesser, 2008).

IV. Findings/Significance - Ethics of Animal Testing – *How is the alternative more effective?*

According to the Humane Society International, 100,000–200,000 animals suffer and pass away each year as a result of aesthetic experimentation. In these tests, chemicals are poured down the animals' throats, into their eyes, and onto their shaved skin to record how they react and confirm that they are safe for human consumption. Your safety through cosmetics may be improved by these studies and testing, but is a chemical reaction in an animal the same as a chemical response in a human?

You might argue that this study and testing is beneficial for your health, but can they anticipate how various consequences will affect various individuals? Do people ever suffer any consequences? \However, because human beings cannot use the results of animal experimentation, doing so has put human lives in jeopardy. In many instances, animal research can injure people in addition to harming animals, according to a fact sheet published by PETA. Some medications were evaluated as safe after being tested on animals, but they nevertheless had negative effects on people. Have we all considered the potential causes of this? The solution is really quite easy. This is due to the stark differences between animals and humans.

With modern technology that we have created these days, animal testing is really unreliable, unscientific and unnecessary experimentation. Nowadays, we have plenty of alternatives which have a much higher percentage of success than animal testing. Instead of animal testing, we can use human cell culture systems; instead of animal testing, we can use computer mathematical models; instead of animal testing, we can use artificial human skin and eyes that mimic the body’s natural properties. "While rabbit tests misclassified 10 of the 25 test chemicals, the company's EpiDermTM approach accurately recognized all irritating substances," according to the article "Cell Culture Beats Animal Tests for Irritancy Accuracy.” This and different investigations show that strategies, for example, EpiDerm or growing cells in vitro can yield results that are identical to creature testing, yet in addition more exact, and even cheaper.

Not only is animal testing ineffective and unreliable, but it is immoral as well. Treatment and cruelty in U.S. laboratories display ethically concerning worries of injustice. Many rabbits, for example, are subjected to the “Drazie Test,” which involves injecting concentrated doses of a test substance into an animal's eye (while its lids are clipped open) or applying a chemical to an area of the animal's skin that is shaved ("Animal testing is Unethical, Unreliable and Unnecessary"). According to Lee, Miri, et al., animals experience "ulceration, inflamed/bleeding skin, enlarged eyes, and blindness" when taking part in an experiment. Lab animals are culled from the wild or produced specifically for scientific

research. They are forced to inhale toxic gasses, imprisoned in withdrawal devices, have holes bored in their heads, or
have their flesh burnt off (PETA). These types of confinements reveal how immoral animals are handled "behind the scenes." Furthermore, a substantial number of animals in American laboratories demonstrate the same torture behaviors as a person would (Akhtar, Aysha). In psychological distress, many animals howl, scream, break their backs in writhing pans, and wrap their arms around their bodies for solace, or rock ("Animal testing is Unethical, Unreliable and Unnecessary"). This demonstrates how animal ethics are ignored when testing is carried out on them. Carried out experiments are out in the name of technical development or pure curiosity at the price of an animal's ability to exist in peace, a right that animals have. Ultimately, this expresses just how immoral animal experiments are.

V. Conclusion (II)

Animal ethics is as important an issue as human welfare. Further efforts are needed to effectively implement the 3 Rs in laboratory animal use. Various alternatives to animal use have been proposed and need to be effectively implemented. This integration requires a variety of computer models, bioinformatics tools, in vitro cell cultures, enzyme screens and model organisms. Analyzing alternative protocol results using modern analytical techniques, data collection, and statistical methods ensures reliable results. These integrated approaches minimize animal involvement in scientific procedures.

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The Importance of Dental Health for all Individuals

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Pubic and Dental Health

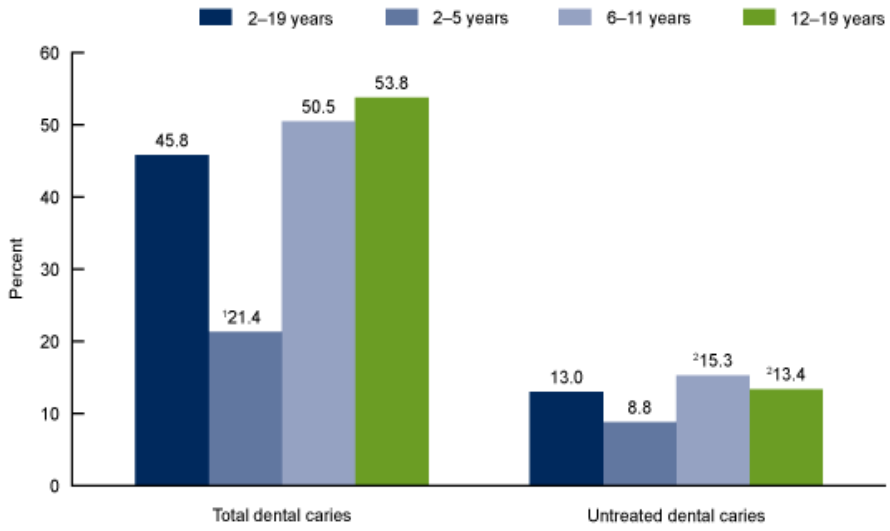
Public health is the science of protecting and improving the health of people within communities. Specifically, this refers to researching diseases and promoting wellness lifestyles. Concepts such as monitoring, surveillance, and analysis are key in ensuring safety amongst a population. The importance of public health continuously increases as there are numerous technological advancements and a new depth of scientific knowledge. Authorities began enforcing protocols as early as the eighteenth century, with the outbreak of the black plague and chickenpox. Just recently, the government placed emphasis on protecting individuals by placing quarantine measures due to the coronavirus. In the last century, it is evident that public authorities have taken a greater role in encouraging healthcare and wellness amongst society. (*National Academy of Sciences, 1988*) Public health covers a lot of community needs. Within the large subject matter, there is dental health. Encouraging dental health and hygiene is important in continuing a healthy life. Public health organizations include the Center for Disease Control and Prevention (CDC), American Public Health Association (APHA), etc. While the national health initiative exists, many people across the world are still unaware of the significance of oral hygiene and the effects it has on one's well-being.

Oral and dental health refers to the health of the mouth: teeth, gums, and the oral-facial system. Awareness of dental health is significant among all age groups. Common oral diseases that people face include tooth decay in the form of cavities, periodontal disease, edentulism (total tooth loss), and oral cancer. Such conditions are largely preventable and can be treated, however, 1 in 5 people are unaware of their dental infections and have untreated dental caries. The lack of pain is one of the key reasons for ignorance in dental hygiene and relentlessness towards dental examinations. Similarly, about 90% of Americans have cavities in their adult teeth and 43% of the adults living in the U.S. have a form of periodontal disease. *(Dr. Jay Khorsandi, December 2022)* According to the National Health Interview Survey released in April 2023, the data for 2022 reveals that only 64.1% of Americans 18 and older have visited a dental clinic in the past 12 months. *(CDC/National Center for Health Statistics, 2023)* Educating adults as well as children on the importance of creating a specific dental cleansing daily routine is essential to keeping an individual's oral health in proper maintenance.

Dental infections

Dental health is important to overall body health. People underestimate the amount of oral bacteria that collects in an individual's mouth. The mouth is the main way that bacteria gathers or gets into one's body system. Dental infections typically begin in the tooth structure and spread throughout the surrounding tissue. The leading kind of dental health problem is tooth decay. This is commonly seen as a bacteria attached to a tooth in the form of plaque. It is the same color as one's tooth, so it can easily go unnoticed. Tooth decay happens on the teeth from different acids within food and drinks, ruining the enamel of the bone structure. This is preventable by focusing on brushing and flossing every day for a minimum of 2 minutes. However, according to dental statistics from 2022, the average American spends 45-70 seconds a day brushing when the recommended time is 2-3 minutes. Likewise, flossing is a major issue amongst Americans as ⅓ floss everyday, ⅓ floss occasionally, and the rest never floss. *(Dr. Greg Grillo, 2022)* This is ineffective and creating more awareness surrounding the importance of spending time each and every day to clean teeth is significant in avoiding tooth decay, especially cavities. Cavities are specifically affecting younger children as parents are not encouraging strong dental habits. Parents justify

skipping a dental appointment or procrastinating, then providing a bad example to their children and future generations.



The prevalence of dental caries as well as untreated caries in 2015-2016
(Centers for Disease Control and Prevention, 2015-2016)

Gum disease is another form of bacterial infection in the mouth. There are various forms of dental diseases, each creating their own levels of pain and effects. An example is gingivitis, which in most cases creates no pain, therefore the disease can go unnoticed. The leading cause as to why individuals ignore their dental health and avoid a check up includes not experiencing any pain. However, there are also other dental infections that are visible or create sensitivity in the mouth: root infections, teeth grinding which leads to tooth erosion, etc. Treating these illnesses are simple with attendance to a dental office. Neglecting oral hygiene creates further issues in one's health and way of living.

Why is oral hygiene ignored?

The dental industry has grown continuously throughout history and will continue to grow in the future as healthcare jobs are necessary in helping to protect individuals' health and wellness. Oral health is not viewed as a top priority for most, though, it is key to prosperity. Encouraging kids to understand the importance of oral health at a young age is imperative. A parent's anxiety and fear of the dentist may influence those ideas onto their kids. It is important to overcome the fear of a checkup. Revealing the significance of attending dental check-ups is important, as most would not prioritize visiting a dentist. For example, an estimated 9% to 15% of Americans avoid dental care due to fear surrounding the experience. In a survey conducted by Randall K. McVey, it was found that fear included the noises of drilling, visibility of tools, fear of pain, shots, self-consciousness resulting from embarrassment of teeth, etc. Dr. McVey has offered ways to get over dental phobia (odontophobia) by using advanced tools such as lasers and sedation for the patients. *(Randall K. McVey, August 2023)* Likewise, as mentioned previously, people do not scrutinize or overthink their oral health as much as they would their body or mental health, especially if no pain is felt. This is seen with dental abscesses. A dental abscess is a collection of pus that is caused by a bacterial infection. *(NHS Inform, 2023)* Abnormal pain is not felt but it is necessary to visit a dentist because they do not go away on their own and could spread to other parts of the body. Mouth

infections have a lack of major symptoms, however, people are unaware of the early signs of an oral infection, limiting them from acting upon their problem.

Symptoms

While some oral diseases do not have severe symptoms or even any at all, if oral hygiene is overlooked and ignorance is prolonged, symptoms can occur. According to Azarko Dental Group Blog, common symptoms include:

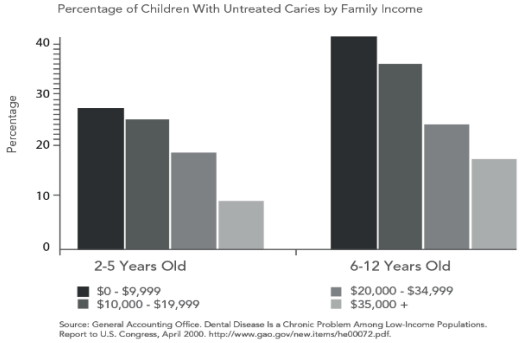
- Sores in the mouth, lips or gums
- Recurring bad breath
- Pain in your teeth, gum or jaw
- Tooth sensitivity to hot or cold foods
- Sore or bleeding gums
- Swelling of the gums, jaw or lymph nodes
- Loose teeth
- Fever
- Headache
- Malaise
- Difficulty swallowing, biting or chewing

Dentists across the world agree that dental health is not being encouraged or prioritized by the government nearly as much as overall whole body health. Specifically, in New Zealand, the average wait time for severe cases was up to 29 days and for children 15 and under, it was up to 131 days. *(Emma Houpt, May 2023)* These adults and children were suffering for months, with no access to basic dental care. In 2022, the World Health Organization (WHO) publicized the amount of oral infections across 194 countries, bringing awareness to the rapid increase over the years. The Global Health Status Report was published revealing that the amount of cases increased over 1 billion in the last 30 years. Untreated dental caries affect about 2.5 million people globally. The report shows the barrier in accessing dental care.

Income correlation/Dental costs

Oral health is expensive and requires large out of pocket expenditures that many people can not afford. More Americans have and prioritize health insurance than dental insurance. There is limited priority for public oral health, and one of the main reasons includes its costliness. Dental procedures can cost thousands of dollars. Basic dental cleanings can be out of pocket ($75-$200) with x-rays for $100-$200 if dental insurance is unavailable or inaccessible. Treatments for dental infections such as crown implementations, tooth extractions, and root canals can vary from $50-$8000. *(Humana, May 2023)*

In reference to income, adults with low-income are twice as likely to get oral infections due to their inability to comply with necessary dental payments. There is an evident strong correlation due to the financial burden it presents. Likewise, regarding the report mentioned previously, it was seen that those within the minority group, those who are older, who do not have quick access to a dentist, etc. are at greater risk. Children are at a disadvantage if their parents or family members are unable to afford dental care and/or incorporate good oral habits. It is their job to create a precedent.



Represents the amount of untreated caries based off of family income

Dental health correlation to other illnesses

Heart attack/blood pressure

Individuals across the world underestimate the significance of oral health to one's overall health. There are examples of the oral bacteria that have correlation to other illnesses. Firstly, Robert H. Shmerling, through Harvard Health Publishing, reveals the moderate correlation between gum disease and heart disease. Individuals with poor oral health have a greater risk of cardiovascular problems and heart attacks. The bateria captured through the mouth travels throughout the entire body, creating blood vessel damage. The inflammation (response) to the bacteria starts the other medical issues. *(Robert H. Shmerling, 2021)* Delta Dental of Washington has found a similar link between oral and heart diseases. A study in 2016 revealed that the risk for heart attack increased significantly amongst people with periodontal diseases with an odds ratio of 1:49.

Gum disease is a form of bacteria or plaque that builds up on teeth, which can contaminate into the blood circulating throughout the body. This then causes blood vessel damage, as well as damage around the heart, leading to cardiovascular damage. For example, a study done by the University of Pennsylvania (PennMedicine) proves that oral bacteria has been found in the fatty deposits of people with atherosclerosis, which can clog the arteries and cause further issues throughout the body system. *(Delta Dental of Washington, February 2023)* While oral bacteria is a leading cause behind heart attacks, there is also a link between oral health habits and low/high blood pressure. Individuals who have poor oral hygiene are more likely to have higher blood pressure or have hypertension (a blood pressure of 130/88 mm or higher). If hypertension is left untreated, it increases the risk of heart attack and death. Poor oral health limits the effects of treatment for hypertension. *(Scott A. Norton, May 2021)* Those with any form of oral disease need their blood pressure to be monitored.

Alzheimers brain disease correlation

A recent study led by the National Institute of Aging (NIA) revealed that bacteria formed from periodontal diseases can lead to the development of Alzheimer's disease and vascular dementia. This was seen in a specific study on older adults, proving that those with oral infections had a diagnosis of dementia. There is a significant difference in the cognitive abilities of older adults with poor oral health compared to those who maintain proper oral hygiene. However, this was a population study, showing association not causation. *(Alzheimer's Association, January 2023)* A specific form of bacteria was found capable of moving to the brain and capable of releasing an enzyme that would destroy nerve cells. Such infiltration of the brain can cause memory loss and the formation of Alzheimer's disease. There must be a significant focus on oral hygiene in order to prevent such diseases or even throughout the early stages of Alzheimer's in order to limit the extent of its severity.

Pregnancy

Descriptions of tooth pain (gingival hyperplasia) were first found in reference to pregnancy in 1817. If oral habits are ignored during pregnancy, gingival inflammation will increase and heighten as there are estrogen and progesterone imbalances. *(Peter J. Robinson & Michael Schmerman, November 2015)* It is essential to maintain good oral health habits, especially for women throughout pregnancy. 60%-75% of pregnant women suffer from periodontal diseases which stay untreated. Likewise, 1 in 4 women who are pregnant (childbearing) have untreated cavities. *(Centers for Disease Control and Prevention, 2022)* Pregnancy takes a great toll on a woman's body, creating irregularity of hormones. Hormones play a major role in dental health. Hormone levels directly affect gum problems and potentially create gum diseases. Build up of oral bacteria throughout pregnancy can also force women to face premature birth, a baby born with a low weight, pregnancy tumors, etc. *(Zeynep Yenen & Tijen Ataçağ, November 2019)*

Conclusion

Dental health is seen as less of a priority to most people across the globe. Less individuals focus on dental health, not understanding its connection to overall wellness. Dental hygiene is costly and can be frightening, leaving people worried and ignorant towards their oral health. The intensity and severe effects of dental infections on one's body cannot be ignored. There has been evident correlation between poor oral health and diseases such as cardiovascular disease, Alzheimer's and problems during pregnancy. Overall, there are clear effects of dental health that are not prioritized by a large percentage of the human population.

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Blood Transfusions: Limitations and Solutions

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Blood Transfusions: Limitations and Solutions

Rachel Nall, a medical freelance writer for Healthline Media, explains how infants are born with approximately 270 milliliters of blood in their bodies (Nall, 2017). As children grow older and bigger, the amount of blood they possess and the probability of accidents and illnesses increases.The red liquid that courses through veins and pumps throughout the body is necessary for human survival. It is essential in delivering oxygen to the brain, thus, supporting life. Nall reports that losing 40%, or 2,000 milliliters, of blood results in death (Nall, 2017). Fortunately, medical processes have been developed and tested to save lives in critical situations. The most common procedure is a blood transfusion. A blood transfusion is when blood from a donor or volunteer is introduced into the patient's bloodstream ("Blood Transfusion" [Mayo], 2022). The process resembles a blood test, where a needle is inserted in a vein, and blood travels through the cannula tube. The only difference is that the IV line sends blood into the body. The University of Rochester Medical Center (URMC) identifies that situations where blood transfusions are necessary are car crashes, surgeries, bleeding disorders, and cancer treatments ("Blood Transfusions in Adults," 2022). The procedure is crucial when accidents result in vast and rapid blood loss, and the urgency depends on the patient's state. Furthermore, the URMC describes how multiple components and types of blood vary based on the recipient and their condition(s). Plasma is the liquid part of the blood. It comprises proteins, water, hormones, and other

substances. Red blood cells (RBCs), white blood cells (WBCs), proteins, and platelets are within the plasma. First, RBCs contain hemoglobin, allowing them to carry oxygen from the lungs to other body parts. Second, WBCs help fight off infections. Third, platelets aid in clotting and stop bleeding from wounds ("Blood Transfusions in Adults"). A patient's blood may lack some of these components, or their condition may call for a specific type of blood transfusion. For example, a person with thrombocytopenia would need a platelet transfusion since their body is devoid of that element and they need it to survive. Moreover, there are four blood groups: A, B, AB, and O. These types represent the antigens that cause immune system reactions in blood cells. There are eight blood types since Rh is a specific antigen, and each group can be positive or negative ("Blood Transfusions in Adults"). Therefore, the type of blood used during the transfusion is crucial because a mix-up can harm the patient's immune system. Even when the correct blood types and components are used, transfusions can cause risks and side effects, explains NHS Inform, one of Scotland's national health information services. These include allergic reactions, incompatibility of cell antibodies, fevers, HIV, and hepatitis B ("Blood Transfusion" [NHS], 2023). Patient reactions, symptoms, and care will vary, and although these conditions are infrequent, they should not be dismissed since the safety rate of transfusions is not 100 percent.

One major problem of blood transfusions is blood unavailability and shortages. This presents both practical and moral issues regarding the medical procedure. First, the supplies necessary to help patients and save lives are not accessible. Second, as blood donations and reserves dwindle, the question of which patients should receive transfusions first arises. So, what factors are fueling these frequent shortages? Mayo Clinic credits the Covid-19 pandemic for blood shortages and a downward donation trend. At the height of the pandemic in 2020, social

distancing and the cancellation of public events restricted donation opportunities. Across the United States, hospitals saw a shift from two-week inventories to two-day inventories within a short period (Stiepan, 2020). Moreover, NPR reports a 10% decline in blood drives since 2020 and a 62% drop in school/university blood drives (Treisman, 2022). Blood unavailability became common due to people's fear of the coronavirus and a concern for their safety. This fear included coming into contact with blood drive volunteers and medical equipment within a perimeter of space. This causes donations to reduce since people are unwilling to attend blood events. Moreover, drives were canceled due to Covid, eliminating the middleman between donors and hospitals and negatively affecting patients who required blood transfusions. The following years were also affected, with people still concerned about their health and costs rising. In 2021, Judy F. Minkove, a senior writer at Johns Hopkins Medicine, interviewed Steven Frank, an anesthesiologist at Johns Hopkins (JHU), and he reported on the hospital's blood costs for that year. JHU spent one million dollars for its red blood cell supply and one million dollars for platelets each month (Minkove, 2021). Hospitals have extensive budgets and supply lists to ensure their patients receive the necessary care. However, spending too much on one component, in this case blood, can throw off this set monetary plan. As supply diminishes and the cost of blood increases, hospitals face the unfortunate circumstance of deciding which situations need the blood the most. A common example of this moral dilemma: Does a premature baby or a single mother in a car accident need the transfusion more? Doctors and healthcare professionals want the best treatment for all patients, but this hope cannot be ensured. Thus, blood unavailability negatively affects both doctors and patients, and donations are essential to provide transfusions to anyone, whenever and wherever he/she/them needs them.

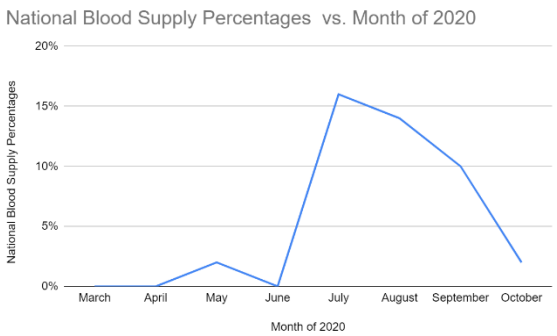

Figure 1: (“Regional Blood Supply,” 2020)

The line graph above depicts the percentages of American blood centers that had a 3+ day blood supply through 2020.

Another major issue regarding blood transfusions is the inadequate detection of infections in blood donations and supplies. These infections are rare nowadays due to improved technology and screening processes, but their existence should not be completely dismissed. If a recipient is infected, the effects are harmful and detrimental. A 2016 Annual UK Serious Hazards of Transfusion article, mentioned by a National Library of Medicine book, reports that bacterial transmission by transfusions accounted for 10% of transfusion-related deaths in the United States. There are two main categories for types of illnesses: bacterial and nonbacterial. One type of bacterial illness is septicemia, which can cause nausea, swelling, chills, unexplained bleeding, and fluctuating blood pressure. One type of nonbacterial illness is hepatitis B, which results in fever, nausea, abdominal pain, and yellowing skin (Buerger and Jain, 2022). These side effects on top of a patient’s pre-existing condition/illness, can take a major toll on their health. Especially since both he/she/they and his/her/their doctor are looking at a transfusion as a viable option to save their life. Therefore, the frequency of transfusion-transmitted infections must reduce. But how are these infections caused? Infectious blood occurs due to the donor’s health or anatomy. The Australian Red Cross describes how blood can be infected during the blood collection procedure due to bacteria in the donor’s skin or pre-existing health conditions

("Transfusion-Transmitted," 2022). Skin is not specifically tested during screenings and this bacteria may not be easily detected since blood is tested for a set number and type of routine and expected diseases. Screening errors are not impossible and can overlook a donor's health eligibility. For example, if a donor has a condition that is not tested for, he may be falsely approved as a "healthy" donor, which in turn, negatively affects potential recipients. So, although screening processes occur before donations and the collection centers are extremely sterile, the complete elimination of potential blood-borne diseases/illnesses is not possible. Another reason blood becomes infected is due to improper storage. The UK report explains how the temperature at which supplies are stored can greatly affect contamination. For instance, for five days, platelet stocks must be stored at 72 degrees Fahrenheit with agitation, a chemical process that ensures the platelets are oxygenated. The CDC also reports how the transmission of infections occurs in every 1 of 2000 platelet transfusions due to this cause. Moreover, errors in transportation, breakages, and improper handling can lead to exposure to contaminants (Buerger and Jain, 2022; "Disease and," 2022). If storage parameters are waved off, or the utmost care is not taken of these blood supplies, they can lead to the development of infections. The incorrect temperatures or locations can promote bacterial and fungal growth. Remember, this is the same blood that will be introduced to an unstable patient's bodily environment and immune system. This idea can be compared to groceries at home. It is fine to leave a pack of potato chips in the pantry due to its composition and makeup. However, a gallon of milk in the pantry leads to its spoiled state and can make people sick if consumed. Overall, detecting blood infections is vital to protecting patient health and improving the safety of blood transfusion procedures.

Once problems are identified, it is easier to develop possible solutions. Scientists, doctors, and experts are working towards reducing the duration and occurrence of blood

shortages. One response involves harnessing technology and academics. In 2021, Stanford University announced the development of a mathematical model that posed an interesting solution. Accounting for blood thickness and flow rate, the experts explained how blood could be substituted with a similar element ("New Model," 2021). By understanding how blood works and is composed, substitutes can be made and distributed to hospitals and patients desperate for transfusion supplies. In fact, as of 2023, blood substitutes, like hemoglobin-based oxygen carriers (HBOCs), are being clinically tested for human use. This new invention's main purpose is to function as hemoglobin and deliver blood to various bodily organs and systems. Advantages of this replacement include a longer shelf life, a reduced risk of infections, and lower financial costs, describes the Pacific Heart, Lung, & Blood Institute ("Synthetic and," 2023). This new technological advancement will help end the increasing demand for real blood by providing other options on the market. It will also help hospitals afford safe and necessary care for their patients. Moreover, the American Red Cross (ARC) proposes that greater community involvement will reduce blood shortages. In January 2022, 68% of hospitals across the United States only had a 3-day blood supply, and ARC estimates that 29,000 blood units are needed daily. Many patients and doctors were under tremendous stress regarding treatments. The renowned organization calls upon the public to make transfusions possible for all. Medical News Today mentions becoming screened donors, attending blood drives, and spreading awareness as viable and impactful ("American Red," 2022). When hospitals and entities cannot obtain blood through transactions or suppliers, they turn to the public and approved donors for help. Citizens who can donate blood must take it upon themselves to help patients in critical conditions and do their part for the community. Along the theme of helping others, different hospitals and organizations should collaborate and share supplies in need. The Harvard Business Review

claims pooled resources can help all hospitals and patients survive blood shortages. (Howard et al., 2022). Cooperation between entities is necessary to deal with blood shortages and ensure proper healthcare. For instance, if a patient in Manhattan needs an emergency transfusion, but the supplies are unavailable, a nearby hospital or clinic should lend the blood or tools. When the medical field is treated as a competition, lives can be lost, so teamwork presents another possible solution to dealing with shortages. In brief, there are multiple responses to frequent blood unavailability that are in use and being developed, indicating that further effort and advancement is necessary to improve the system of blood transfusions across America.

Methods and responses are also being developed to prevent transfusion-transmitted infections. Fairly recently, pathogen inactivation technology has been helping reduce the risk of transferred infections, explains the AABB Pathogen Inactivation Technology Review Work Group. In 2017, the Food and Drug Administration (FDA) approved pathogen inactivation, which is still used today. It consists of "treating" the blood to rid it of any infectious agents upon collection—this method represses the virus's ability to replicate. When amotosalen, a chemical agent, is activated by ultraviolet light to bind nucleic acids, the DNA cannot replicate ("Questions, 2017"). The success of this method is apparent through its common use today. It helps ensure "clean" blood for patients, prevents them from exposure to infections, and saves their immune systems from further strain. Moreover, in January of 2023, the FDA proposed guidelines and questions that should be added to blood donor registration questionnaires. These proposals include blood establishments performing required blood testing for infections, asking donors about their past sexual partners, and recording their history with HIV and HIV medication ("FDA Proposes," 2023). These measures will help reduce the likelihood of transmitted diseases. By promoting blood testing, health professionals will be certain if the blood

is eligible for transfusions and helping patients. The sexual and HIV questions will help crack down on the transfer of HIV to possible patients and ensure optimal quality blood donations. Along with updated donor questionnaires, the Association for the Advancement of Blood and Biotherapies ("AABB22," 2022) reports that new questions include asking donors about any existing blood deficiencies/disorders, and tool kits will be administered to blood collectors and centers to ensure proper transfusions. AABB is currently awaiting approval from the FDA ("AABB22," 2022). Donor applications are necessary to approve or reject blood volunteers to ensure the safety of future transfusions and patients' health. Asking about a donor's blood disorders helps determine if the patient can handle donating blood and ensure their safety. It also avoids transferring infections/deficiencies to recipients. Moreover, these tool kits will provide blood collectors with new equipment and make receiving blood easier. In short, approaches to reducing the risk of transfusion-transmitted infections are underway and still being developed.

Blood transfusions are an important medical process in dealing with a patient's health conditions, both long-term and life-threatening. Along with the benefits come disadvantages and external factors that affect their success and positive effects. These include blood shortages and transmitted infections, which hinder the provision of proper healthcare. Fortunately, solutions are being developed to help improve the dependability and distribution of transfusions. However, these advancements are only possible through the collaborative efforts of experts, scientists, healthcare professionals, and community members.

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A Comparative Study of Machine Learning Approaches for Enhancing Copyright Protection Strategies

Audrey E. Ng

Abstract

In recent times, businesses have become more subject to copyright infringement due to the widespread accessibility of digital content and the ease of unauthorized reproduction and distribution. As a result, businesses lose customers and money to their plagiarized counterparts. In order to mitigate these effects, machine learning techniques can be utilized to detect plagiarized content. This paper aims to present and evaluate the effectiveness of various machine learning approaches in enhancing businesses' copyright protection strategies, including Support Vector Machines, Random Forests, and Convolutional Neural Networks.

Keywords: artificial intelligence, machine learning, copyright infringement, copyright protection, support vector machines, random forests, convolutional neural networks, intellectual property, plagiarism detection

Literature Review

Copyright protection is a crucial concern for businesses that create and distribute intellectual property. With the exponential growth of digital content and the rise of online piracy, traditional copyright protection methods are becoming insufficient. For instance, stamp-set designs can easily be copied and rebranded as a separate (and usually cheaper) product. Customers looking to buy the original stamp-set designs may be deceived by the copied products' design and attracted by the lower cost which may lead them to opt for the cheaper price instead. The traditional method of addressing these copied products is to manually analyze the similarities of the products and individually report those that do. However, with the rise of artificial intelligence, specifically machine learning, businesses now have the opportunity to address copyright infringement concerns in a more efficient manner. The following literature review attempts to understand the existing research and advancements in the field of copyright protection and machine learning.

Several studies have demonstrated the effectiveness of machine learning algorithms in detecting and identifying instances of copyright infringement. A study by Lelisa Adeba Jilcha and Jin Kwak (2022) emphasized the use of machine learning algorithms to detect advertisements served on suspected piracy websites. Just like original designs, online advertisements can easily be copied and reuploaded on a separate website that claims it to be their own. This action directly affects businesses and can cause billions of dollars lost in revenue. The proposed technique to address this issue involved the implementation of two models: support vector machines (SVMs) and a word2vec vectorization model. A support vector machine is a machine-learning algorithm that analyzes data to classify them into groups. The word2vec vectorization model takes words from a text and converts them into numerical vectors which represent the meaning or context of the words in a way that a computer can understand. The evaluation of this proposed technique found that their trained model can achieve an impressive 97% accuracy in identifying advertisement banners from piracy websites.

Similarly, a study by Kim et al. (2021) explores the use of a photo identification framework in protecting intellectual property from manipulations. The photo identification framework consists of various image-processing techniques that facilitate the extraction of distinctive features and patterns. The authors leveraged a training dataset with a wide range of authentic and manipulated images, which allowed their model to gain the ability to identify new differences between the two categories. The study also highlights the framework's adaptability across various industries and domains. Its potential applications extend beyond conventional product counterfeiting concerns to encompass image tampering

in fields such as journalism and forensics; the versatility of their approach demonstrates that it is a useful tool in the ongoing battle against digital fraud and misinformation.

These studies demonstrate the potential of machine learning techniques in identifying instances of copyright infringement. From identifying copied designs to shielding brand reputation against counterfeit products, the applications of machine learning are already showcasing their capability to detect and counteract copyright violations. As businesses navigate the evolving landscape of intellectual property rights, utilizing machine learning techniques serves a dual purpose: preventing copyright infringements and cultivating consumer trust. This not only upholds fairness but also contributes to sustained competitiveness in the market. Additionally, the intersection of technology and copyright protection offers a key avenue for businesses to uphold their creative endeavors while preserving fairness and authenticity in their intellectual property.

Methodology

The traditional method of combatting copyright infringement is to manually identify plagiarized content and report each product individually, which can be tedious. To make this process easier, this research aims to present various machine learning techniques that could reduce the manual effort of identifying such content when implemented on a trained model. It is important to note that the solutions outlined in this paper are hypothetical and have not undergone empirical testing.

Support Vector Machines

By utilizing a machine learning algorithm called support vector machines (SVMs), a trained model can learn patterns and features from a labeled dataset consisting of both genuine and plagiarized content. The model can then establish a decision boundary that distinguishes specific categories.

The SVM's mechanism involves transforming data points into a higher-dimensional space, which allows the model to identify optimal hyperplanes that differentiate categories. This process is guided by "support vectors," key data points that are close to the decision boundary. The SVM then learns to generalize patterns and classify new data points.

The classifier function is defined as $f(x) = w \cdot x + b$. In this equation, $f(x)$ represents the classifier's prediction for the given data point x, w represents the weight vector associated with the decision boundary, and b represents the bias term, which is an adjustment that helps position the decision boundary in a way that improves how well it separates different categories. It is important to note that there is a lot more information regarding how a support vector classifier works. However, **Figure 1** depicts a general representation of the classifier function.

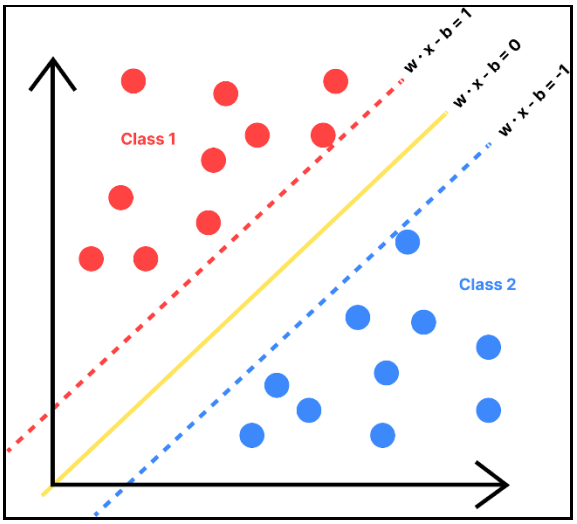

Figure 1. Graph of the support vector classifier function.

Random Forests

A random forest is a machine learning technique that involves constructing a group of decision trees that collaborate to make decisions. Each decision tree is trained on different subsets of a dataset. Random forests excel in their ability to handle diverse and complex datasets due to the use of multiple decision trees. Having multiple decision trees enhances generalization and mitigates the risk of overfitting, which occurs when a model performs poorly when given new data despite its strong performance on the training dataset.

As shown in **Figure 2**, The key process within random forests is the creation of individual decision trees and the subsequent fusion of their decisions. Each decision tree contributes its own insight by learning distinctive patterns from a subset of data and a random selection of features. The group of decision trees as a whole then integrates these insights to deliver a collective, final decision.

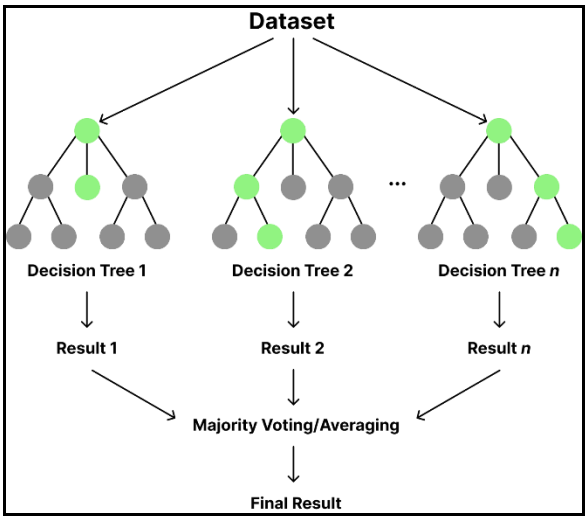

Figure 2. Random forest algorithm process.

Convolutional Neural Networks

A neural network is a machine learning model inspired by the connections between neurons in the human brain. Its framework comprises layers of interconnected nodes, or “neurons." These nodes process information and learn patterns from data.

A Convolutional Neural Network (CNN) is a type of neural network comparable to the human brain’s ability to recognize patterns and features in visual stimuli since they start by using layers called "convolutional layers" which learn and extract features from visual data by applying small filters that detect patterns like edges and textures across it. Convolutional layers are followed by "pooling layers" that downsample the features, which reduce their spatial dimensions and in turn make the network more efficient. Finally, fully connected layers combine the learned features and make decisions. The hierarchical structure of CNNs allows them to learn simple features in early layers and more complex features in deeper layers, making them useful for tasks such as image recognition.

Discussion

This paper proposed several machine learning techniques that reduce the manual effort of identifying plagiarized content when implemented on a model. In this discussion, these techniques will explained regarding their benefits to aid businesses in the copyright protection process along with their potential limitations. Again, the solutions outlined in this paper are hypothetical and have not undergone empirical testing.

Support Vector Machines

As illustrated in **Figure 1**, a support vector classifier function has the ability to establish a decision boundary that differentiates between different classes. Therefore, in the context of copyright

protection, SVMs can be trained using labeled datasets that contain both copyrighted material and potential infringements. Once trained, these models can classify new and unseen content while also flagging items that may require further human review.

Businesses can utilize SVMs to build automated systems that monitor digital platforms for unauthorized use of copyrighted material. For example, SVM-based algorithms can be employed to scan websites, social media platforms, and content-sharing platforms for instances of content that closely resembles copyrighted works. By setting appropriate thresholds, SVMs can help identify content that may be infringing on copyrights. Integrating SVMs would also save businesses the time and effort that would typically go into manually identifying infringing content.

However, it is important to consider the potential limitations of SVMs. If the dataset that an SVM is trained on is too large, the SVM could become computationally intensive and memory-demanding, which could delay the infringement detection process. If the dataset is unbalanced (too much of one type of content) or contains data that is incorrectly labeled, the SVM is likely to incorrectly classify new content. Therefore, if a business does decide to utilize an SVM, the dataset they use to train the SVM should be of a manageable size, balanced, and accurate.

Random Forests

Random forests can be trained using labeled datasets containing copyrighted and non-copyrighted content. Multiple decision trees allow random forests to capture complex patterns within the data, making them effective at distinguishing between different types of content.

Businesses can leverage random forests to build predictive models that determine whether a given piece of content is original or plagiarized. These models can consider a variety of features associated with the content, such as text, images, metadata, and more. The random forest algorithm is also capable of automatically selecting relevant features and learning complex relationships between them, which is particularly valuable when dealing with diverse forms of content that may have varying infringement indicators. Unlike SVMs, random forests are well-suited for handling unbalanced datasets, which are common in copyright protection scenarios since there may be more cases of infringing content than original content. They can also assign appropriate weights to different classes which ensure that both infringing and genuine content are accurately identified. This is crucial for reducing false positives and negatives in copyright detection. Since the random forest algorithm also includes a feature where a collective decision is made between the different decision trees errors determined by individual decision trees do not have much influence on the final decision. Thus, the risk of overfitting (when a model performs poorly when given new data despite its strong performance on the training dataset) is reduced.

While random forests can effectively handle datasets that are unbalanced and contain inaccurate classifications, one drawback is their computational complexity and memory requirements, especially with large datasets. Utilizing the random forest algorithm involves training multiple decision trees, which can become time-consuming and resource-intensive when processing large datasets. This could lead to slower response times in real-time monitoring scenarios and affect how fast businesses can identify and address violations.

Convolutional Neural Networks

Convolutional neural networks excel at image and pattern recognition, which is particularly useful for identifying copyrighted content and potential infringements within images and videos. By training CNNs on labeled datasets containing copyrighted material and non-copyrighted content, businesses can create models that learn distinct visual features, such as unique textures, shapes, and arrangements. Learning these features allows CNNs to identify subtle differences between original content and unauthorized reproductions, even when transformations or alterations have been applied. As with the other machine learning techniques, CNNs can enhance the efficiency of copyright monitoring by automating the process of content analysis which, in turn, saves businesses time and energy.

While CNNs offer remarkable capabilities for copyright protection, one limitation is the need for large amounts of labeled training data. Developing accurate CNN models requires extensive datasets containing both original and infringing content, which can be time-consuming and resource-intensive. This can pose challenges for businesses, especially those with limited access to diverse and well-labeled training content. Additionally, the complex architecture of CNNs can make them computationally demanding and require powerful hardware resources for efficient real-time analysis. Not every business has access to these resources.

Conclusion

This paper explored the potential of three machine learning approaches: Support Vector Machines (SVMs), Random Forests, and Convolutional Neural Networks (CNNs). These techniques offer different advantages in detecting and mitigating copyright infringement across various forms of content. SVMs excel in creating decision boundaries to classify different categories, while Random Forests leverage ensemble learning to handle complex and diverse datasets. CNNs have the ability to identify intricate visual patterns and features that distinguish original content from infringing content. While each of these machine learning techniques has its benefits, their implementation comes with certain considerations: selecting appropriately sized and balanced datasets, dealing with computational demands, and ensuring access to powerful hardware resources for efficient real-time analysis. By adopting these techniques, businesses can enhance infringement detection, preserve brand reputation, and improve their consumer trust. These advancements offer a path towards more efficient and effective intellectual property safeguarding, especially in an era with rapid digital creativity and widespread content sharing.

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