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NO LIMITS

The Hotchkiss School
2025 Issue

Is IRON FERTILIZATION the KEY to
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The How of Hotchkiss Keycards

Article by Dwyer Illick '26



Figure 1: Deconstructed Keycard

When these keycards are held up to one of the door scanners on campus, the scanner either flashes green and unlocks the door or flashes red and denies access. Every time a keycard is brought close enough to a scanner, it transmits its unique, identifying signal back to the scanner. Hidden beneath the physical card and scanner is a third, invisible component. That component is a database operated by the Security office, that connects the unique signal of every card to the identity of a student or faculty at Hotchkiss. This database knows the level of access each keycard has. When a keycard connects with a doorside scanner, the scanner cross references the keycard's signal with the information in the database to determine whether or not to unlock that door. When Hotchkiss Security needs to create new cards for students, they first order a batch of blank keycards, then print the name and face of the student on the card.

These cards come with their unique signal pre-encoded, so the team at Security simply has to scan each card into the database, and specify the student's level of access (C. Eaton, personal communication, December 9, 2023).

Sixteen months ago, I arrived on campus for the very first time as an official Hotchkiss student. After awkwardly making my way through the barrage of cheering from older students dressed in Bearcat costumes, I took my first steps into the MAC's fieldhouse. In the fieldhouse, smiling faculty members ushered me towards a desk where a complete stranger casually handed me a brand new, thousand-dollar computer with my name on it. I then moved on to the next station.

Here, some lady gave me a small plastic rectangle that she claimed would be my lifeline at this school. She told me to bring this little white card with me everywhere and be careful never to lose it. At the time, I couldn't see what this rectangle had to offer beyond a very unappealing photo of my face.

Looking back, I now see how wrong I was to underestimate it. Often referred to as the "One Card," this piece of plastic served as my wallet, my means of identification, and the key to every building at Hotchkiss for my Prep year. Earlier this fall, I realized that despite the frequency with which I use my One Card, I had no clue how it actually managed to unlock doors and transfer money. On top of that, the keycards can operate without a battery, as they never lose power or need a recharge. I have since descended deep into the rabbit hole of what makes these magical little keycards tick.

The keycards transmit data to the scanners via RFID (Radio Frequency Identification) technology. In any RFID system, a reader component sends out radio waves to a tag component that transmits its unique signal back to the reader.

Our Hotchkiss keycards serve as the tag component in this system. RFID tag components capture the reader's radio waves with an antenna, which prompts the tag to transmit its data. The card's unique identifying code is stored on a microchip within the card. The miraculous thing about certain RFID tags is that they don't require a power source, as its antenna simply harvests the energy of the reader's radio waves.

While some versions of RFID tags do need a battery, the RFID tags in the Hotchkiss One Cards do not, and are called 'passive' RFID tags. However, this method doesn't provide enough energy for the tag to generate its own radio signal, so the RFID tags resort to a technique called backscatter modulation (Wireless and Mobile, n.d.). RFID tags implement backscatter modulation by adjusting the load impedance of their antenna. Load impedance refers to the electrical resistance of the antenna. The electrical resistance of the antenna affects how much of the scanner's original electromagnetic signal is reflected back towards the reader, and how much is absorbed by the tag (Nagaraj, 2017). The RFID reader can measure when the tag's antenna is switched to a high impedance, and when it is switched to a low impedance. By rapidly oscillating between these two states, the tag's antenna transmits binary data with high impedance representing a 1, and low impedance representing a 0.

This technology used by the Hotchkiss Keycards is a close cousin of the tech behind Tap-to-Pay credit cards, Apple Pay, and Apple's new NameDrop feature. These work by using NFC (Near Field Communication), which is a subset of Radio Frequency Identification.

Just like the RFID cards described above, these NFC based technologies transmit information along radio waves, but there are a few key differences. One significant similarity is that NFC tags can operate without a battery, and use the same method as RFID tags of repurposing the energy emitted from the reader component. Instead of utilizing the backscatter modulation technique, NFC tags and readers generate a single, shared magnetic field. The NFC tag then modulates that magnetic field in a specific way, which the reader component can detect. The difference here is that NFC tags modulate a shared magnetic field, whereas RFID tags modulate the radio waves that backscatter off of them.

A tag and a reader need to be much closer together to generate a shared magnetic field than they do to bounce radio waves back and forth, so NFC has a more limited range than RFID cards. This limited range functions as an advantage in the case of Tap-to-Pay credit cards, as it makes it more difficult for malicious third parties to intercept the transmission. iPhones can act as both an NFC tag and an NFC reader, which makes two way communication possible.

Understanding RFID and NFC technology clarified a lot of questions that have been bouncing around in my head for a while. For one, I was always confused last year why the Snack Bar had to have separate scanners for people paying with their One Card and people paying with credit cards or Apple Pay. Now it's clear to me that one of these scanners must have been built for communicating in the range of the RFID keycards, while the other was built for generating shared magnetic fields necessary in NFC communication. Most iPhones are equipped with NFC tags and readers, but none for RFID.

This is how Apple Pay on iPhones can act as a regular Tap-to-Pay credit card using NFC, but cannot take the place of our One Cards yet as the door locking system is built with RFID readers. Over the course of my time at Hotchkiss people have occasionally warned against using a wireless charger on an iPhone if a One Card is stored in the case. The reason people warn against this is because the wireless charger's high power output can overwhelm the RFID tag within the card. The antenna within the RFID card can intercept the charger's energy that was intended for the iPhone, and fry its own circuits in the process (How to Wirelessly, 2023).

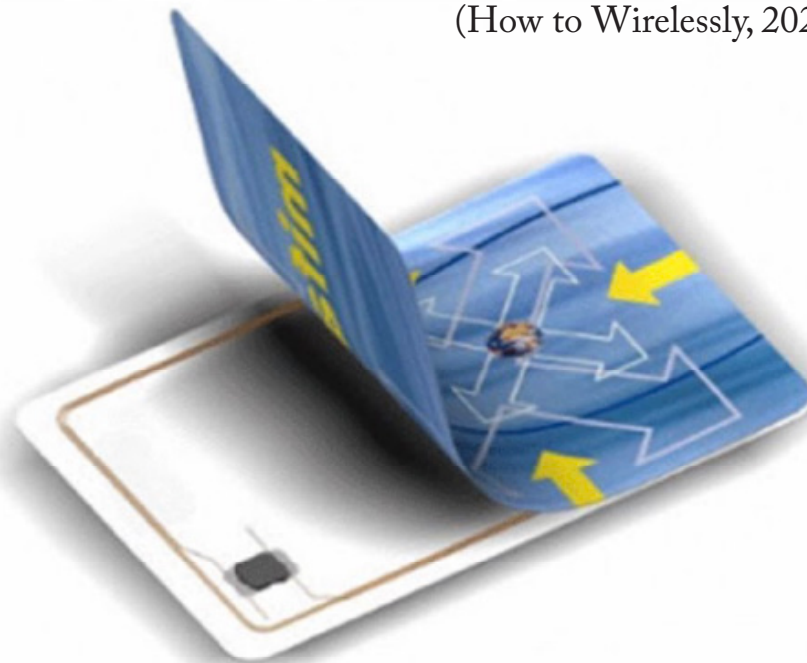


Figure 2: Alternate Perspective of Deconstructed Keycard

You may be feeling now that it would really be better if Hotchkiss went back to a simpler time. Back to a time when people only used good old fashioned metal keys and locks. Maybe you would sleep better at night if the safety of your school didn't depend on invisible things like backscatter modulation and load impedance. Or maybe you've heard too many cases of people cloning RFID keycards. Christian from Security is here to comfort you about the reliability of Hotchkiss's RFID keycard system. When I asked him for his thoughts on the safety of our current keycard system, Christian responded, "I'm confident in the fact that nobody that doesn't have a card in this system tied to their name is (...) going to randomly get access to a dorm." Christian's emphatic profession of trust in our keycard system gives me comfort as my safety depends on RFID technology.

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Is Iron Fertilization the Key to Tackling Climate Change?

Article by **Chloe Kong '28**

In 1953, 6 billion tons of carbon dioxide (CO₂) were emitted. By 2023, this number had sextupled, emitting over 36 billion tons. Since then, carbon emissions have continued to grow at an alarming rate, with no end in sight.

Why do we care?

Carbon dioxide emissions constitute approximately 76% of total greenhouse gas emissions worldwide. These gases absorb infrared radiation and trap heat within the atmosphere. Following the current trajectory, carbon emissions will only continue to increase, leading to even greater concentrations of greenhouse gas. Global warming refers to the global increase in surface temperature that occurs as a result. The consequences of global warming are far-reaching: loss of biodiversity, rising sea levels, coral bleaching, poverty, malnutrition, increased and severe storms, droughts, and wildfires, among other disastrous outcomes.

How might Iron Fertilization solve this problem?

However, recent studies suggest that iron fertilization may be a possible solution to the carbon emissions problem. Unlike other practices that target the human sources of pollution, such as reducing waste and converting it to renewable energy, iron fertilization addresses CO₂ emissions by directly removing the gas from the atmosphere after it has been emitted. In the bigger picture, this shifts the focus from prevention to mitigation. Iron fertilization targets one of the Earth's greatest natural carbon sinks: the ocean. The idea is to introduce iron-containing compounds, like iron sulfate, into parts of the ocean where it's scarce. This would spark massive blooms of phytoplankton, a type of microscopic marine algae that can absorb, transform, and recycle elements such as carbon, nitrogen, and phosphorus. Phytoplankton absorb carbon from the atmosphere through photosynthesis, and when they die, sink to the bottom of the sea. This ultimately sequesters the absorbed CO₂ in the seabed for decades.



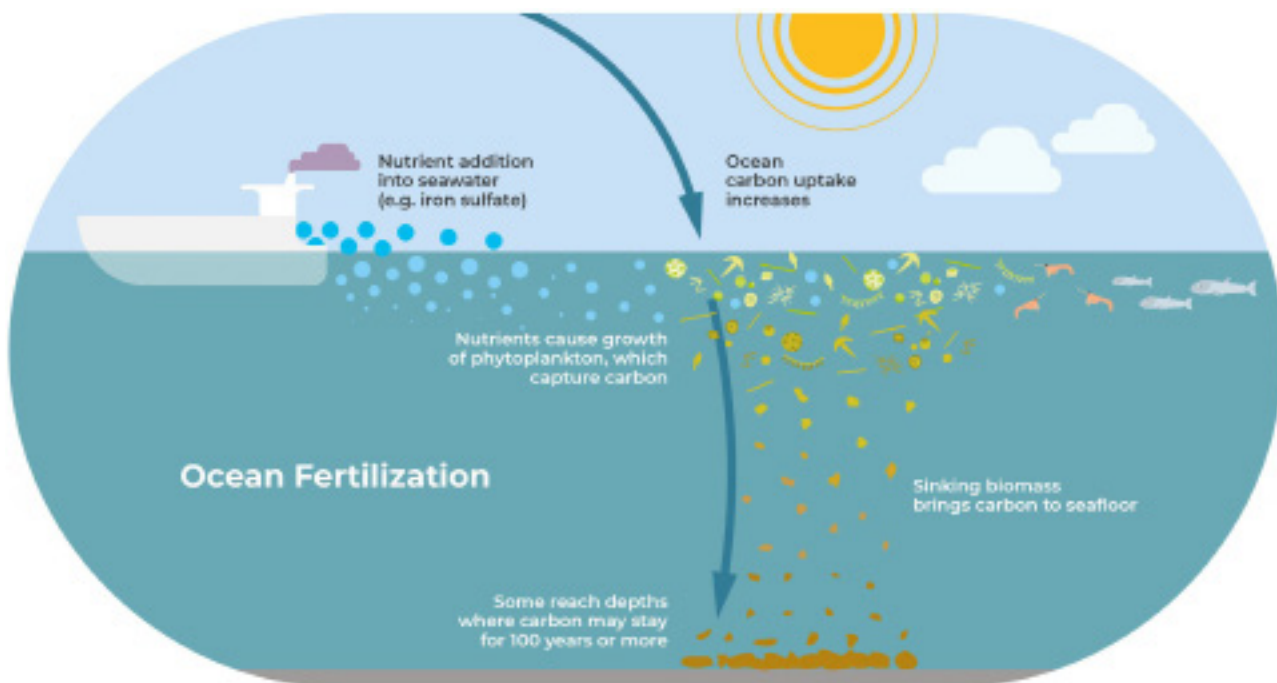


Figure 1: Visual of Ocean Fertiliation

What are the Implications?

While iron fertilization is promising, it remains controversial partly because its full effects on the marine ecosystem are poorly understood. Scientists believe that side effects might include the disruption of the ocean's nutrient balance—the cornerstone of the ocean's food web—the creation of anoxic conditions, and a dramatic increase in the demand for iron, which could potentially incur environmental damage. Historically, the technique's efficacy has been questioned for decades. Since 1990, thirteen major have been carried out to evaluate the efficiency and possible consequences of the technique. The results were mixed, with some experiments demonstrating increased phytoplankton growth and significant carbon sequestration, while others showed limited carbon export to the deep ocean. These findings suggest that there is still work to be done. Before it can spearhead a widespread climate initiative, iron fertilization will have to prove its reliability in future experiments.

How should we move forward?

Considering all the potential negative side effects, many think it is unreasonable to continue investing in this endeavor, with the fear that iron fertilization will divert attention focused directly on reducing carbon emissions. However, the potential that iron fertilization has in extracting CO₂ remains intriguing and is worth the time and effort for further research.

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Optimizing Light Exposure to Alleviate JetLag: Understanding Circadian Rhythm Adjustment Strategies

Article by Yaoyao Yuan '27

Introduction

This paper is inspired by my own experiences in battling jet lag. The time and effort required for me to adjust to a new time zone varies from time to time, inspiring me to find the underlying reasons and patterns of these differences. By doing so, I can help others who travel frequently to find the most efficient way to combat jet lag. I began this pursuit by recording my sleeping hours, sleeping quality, feeling of tiredness, caloric intake, melatonin intake, and sunlight exposure of traveling days for the past three travels to a significantly different time zone (6 hours or more). The trends were unexpected. My sleeping quality the first night I landed and my energy levels the day right after do not correlate at all with the number of hours of sleep I got on the plane. Caloric intake did not affect my sleeping quality and energy levels either. Interestingly, if I purposefully wake up early in the morning on the day of the flight and use the reading lights on the plane a lot, I sleep much longer the night I land and have much higher energy levels the day after. The results if I stayed up throughout the night before the flight and slept during the day were the opposite. This clear trend leads me to hypothesize that light exposure plays a pivotal role in regulating the circadian rhythm and adjusting to a new time zone. Meanwhile, this observation aligns with the well-established scientific understanding that light is the primary external cue or zeitgeber for the circadian clock mediated through the brain's suprachiasmatic nucleus (SCN). In this paper, I aim to explore the connections between light exposure and jet lag adaptation by conducting literature reviews on the biology of circadian rhythms, analyzing case studies of travel data, and synthesizing these findings into practical

Mechanisms of the Circadian Rhythm

When light enters the eye, it reaches the retina, where it interacts with photosensitive retinal ganglion cells (ipRGCs). Once ipRGCs detect light, they send electrical signals through the retinohypothalamic tract (RHT) to the supra-chiasmatic nucleus (SCN), a bundle of neurons located at the roof of your mouth.

In response to light signals, a series of molecular interactions that determine your circadian rhythm, also known as your sleepiness and wakefulness cycle, occur in the SCN.

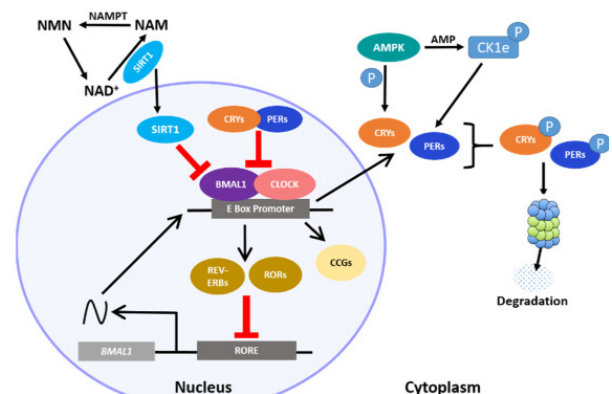


Figure 1. Transcriptional-translational feedback loops regulating the mammalian circadian clock.

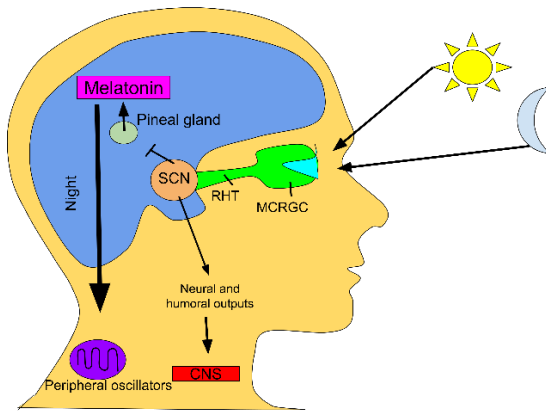


Figure 2. Light input regulates melatonin production and circadian rhythms in the human brain.

In this process, the CLOCK and BMAL1 proteins form heterodimers (molecular pairs) that bind to specific DNA regions, activating the transcription (or expression) of Per (Period) and Cry (Cryptochrome) genes. Once Per and Cry proteins accumulate, they form complexes that inhibit the CLOCK/BMAL1 activity, thus reducing their own expression in a negative feedback loop. Per and Cry are eventually degraded, allowing CLOCK/BMAL1 activity to resume, thus restarting the circadian cycle (Nakao et al., 2015).

The synchronized, highly interconnected neurons in the SCN oscillate and transmit their rhythm to peripheral oscillators such as liver, lung, and kidney via neuronal, neuroendocrine, and behavioral pathways. This circadian cycle entrains physiological processes including the sleep-wake cycle, liver metabolism, and body temperature (Narasimamurthy & Virshup, 2017). This cycle could also be reset with and only with exposure of light to the eyes.

The Key to Clock Control: Understanding Your Temperature Minimum

Causes of Jet Lag

Jet lag occurs because the internal circadian clock becomes misaligned with the new local time after crossing time zones. Specifically, the suprachiasmatic nucleus (SCN) and reinforced by the cyclical interactions of CLOCK, BMAL1, Per, and Cry proteins, continue to operate on the old time schedule, even in a new time zone. However, since these series of molecular interactions are responses to light signals to the eyes, intentional exposure to bright light at a specific time may accelerate the shifting of the circadian clock such that the circadian misalignment is minimized and the severity and the duration of jet lag could be reduced.

Body Temperature and the Sleep-Wake Cycle

The core body temperature decreases during the nocturnal sleep phase and increases during the wake phase repeatedly in a 24-hour circadian rhythm (Okamoto-Mizuno & Mizuno, 2012)

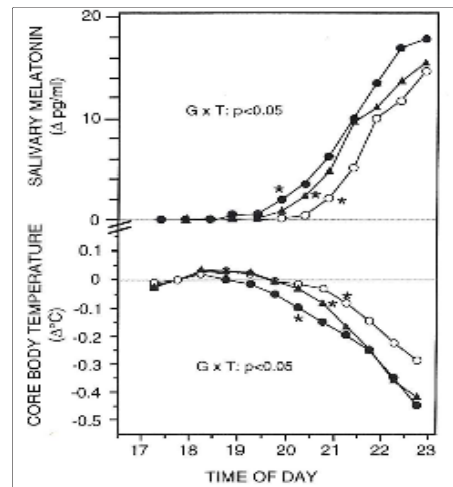


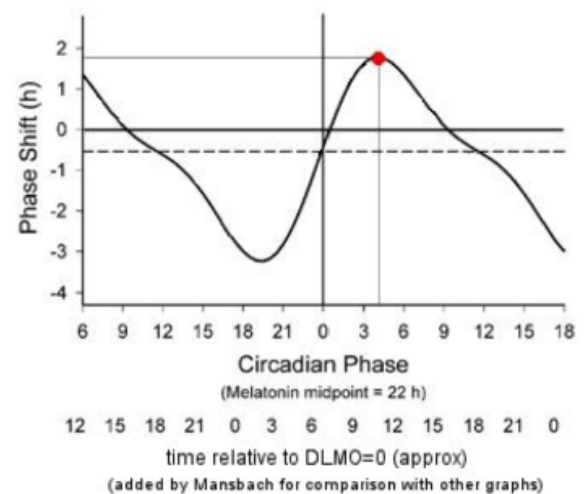
Figure 3. The Correlation Between Core Body Temperature and Salivary Melatonin, With the Time of the Day.

Temperature Minimum

By understanding the timing of your temperature minimum and strategically using light exposure, you can shift your circadian rhythm to align with your new time zone more quickly by performing phase advances and phase delays. Temperature minimum is the point in every 24 hour cycle where your temperature is the lowest, and this point of time varies from person to person. A general rule of thumb is that temperature minimum occurs 1.5-2 hours before your average wake-up time.

If you expose your eyes to bright light in the 4 hours after your temperature minimum, your circadian rhythm will shift so that you will tend to go to bed earlier and wake up earlier in the next few days. This is called a phase advance, where you advance your clock. For instance, if you wake up at 7:00 AM your temperature minimum occurs around 5:00 AM, light exposure between 5:00 AM and 9:00 AM will make it easier to go to bed and wake up earlier over the next few days, which is useful when traveling eastward.

In contrast, if you expose your eyes to bright light 4 hours before your temperature minimum, you will tend to sleep



Phase Response Curve for 6.7 hour white light exposure

Figure 4. Phase Response Curve (PRC) for 6.7-Hour White Light Exposure.

later and wake up later and thus experience a phase delay. This means if your temperature minimum is around 5:00 AM, light exposure from 1:00 AM to 5:00 AM will make it easier for you to stay up later and wake up later. This strategy is beneficial for westward travel (Mansbach, 2021). This graph shows light on awakening advancing one's circadian clock by nearly 2 hours (red dot) with 6.7 hours exposure to light after minimum temperature achieved, and a forced advance of sleep time.

Conclusion

To conclude, when traveling across significantly different time zones, understanding your temperature minimum and the direction of travel can help you adjust to jet lag more effectively. For eastward travelers, phase advances are key—this involves exposing yourself to bright light after your temperature minimum. In contrast, westward travelers benefit from phase delays by exposing themselves to light before their temperature minimum. These strategies correspond to biological mechanisms of the suprachiasmatic nucleus discussed above, and provide practical ways to reduce the severity and duration of jet lag.

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A CRISPR Tomorrow: Genetic Engineering & The Future of Medicine

Article by **James Zhou '28**



Imagine that a young boy is diagnosed with a rare genetic disorder; frequent seizures and developmental delays threaten his life. Doctors try their best, but over time, the boy's condition only worsens—until he becomes one of the first patients treated with a frontline technology named “CRISPR.” A few months later, he is living seizure-free for the first time and looking at the future with renewed hope.

Overview

CRISPR—“Clustered Regularly Interspaced Short Palindromic Repeats”—had not just given the hope of a workable remedy to countless suffering patients like this boy but also presented the hope of a fascinating, groundbreaking study to the entire science and medical community. In an overview, CRISPR is a modern gene-editing technology that allows scientists to genetically engineer and modify specific strands of DNA. In the targeted cell, scientists send the CRISPR to specific locations and replace the mutant genetic material with the CRISPR strands, which would rectify the cell's original erroneous DNA with the correct ones (edited through CRISPR) and, therefore, cure the genetic disorder or disease once the sequence is accurate again.

The landmark discovery and proficient use of this technology was initiated just a decade ago, in 2012; however, the history of CRISPR is rather a unique journey that can be traced a few decades earlier. In 1987, CRISPR was discovered in *E. coli* by a Japanese scientist named Yoshizumi Ishino and his team, who accidentally cloned these peculiar sequences when analyzing a gene, but were not aware of the function of those arrays due to insufficient data of the DNA sequence. In 1993, researchers in the Netherlands led by J. D. Van Embden took a more rigorous analysis of the spacer sequences between the DNA repeats, specifically examining the *Mycobacterium tuberculosis*, and were the first to refer to them as “CRISPRs.” What the two previous experiment ideas hinted at is that rather than an artificial technology, CRISPR was actually a natural defense mechanism that already exists in bacteria, and it would bring unimaginable impact if it could be applied to human genomes. CRISPR pioneer scientist Jennifer Doudna reflects, “Nature has a lot to offer and much of it is likely better than anything we could imagine. Hidden inside some of the world's smallest organisms is one of the most powerful tools scientists have ever stumbled across” (What is CRISPR? - Explained by Jennifer Doudna & IGI Expert, 2024). Finally, after another few years of attempts and experiments, a team of scientists mainly led by Jennifer Doudna and Emmanuelle Charpentier in 2012 refined CRISPR's usage and harnessed it as a gene-editing tool that can safely and accurately modify the targeted genome regions. CRISPR was named the “Breakthrough of the Year” in 2015 and eventually earned the two leading biochemists the Nobel Prize in chemistry in 2020.

The CRISPR Gene-editing Process

Although CRISPR is already a sophisticatedly developed and complex mechanism derived from bacteria, some critical modifications still need to be added to make this technology applicable for targeting specific issues in the human genome. One such groundbreaking renovation was the invention of the “Cas” systems, or CRISPR-associated proteins or nucleases. Together with the CRISPR technology, the CRISPR-Cas systems create an adaptive immune system that protects the cell when invaders are inserted and can cut the foreign DNA into fragments. When applied to correct human DNA and gene sequences, the scientists first identify which region is problematic and send the CRISPR-Cas protein to the site, which is guided by another component — the “single guide RNA” (sgRNA). Then, the Cas endonucleases will come in handy and effective as they will perform the primary “surgery” on the gene sequence, such as binding to the site, cutting out the erroneous sequence, replacing it in the correct sequence, and natural degradation after completion. In this clear-cut plan, CRISPR delivers a miraculously direct method to tackle genetics-related diseases. Normally, illnesses like infectious diseases are dealt with by an innate immune system and are less likely to be a persistent concern. On the other hand, genetic diseases are rooted in a different dilemma: the genes. The symptoms and disorder are not going to fade away if the gene sequence is not repaired, corrected, or completed. Hence, CRISPR has become a perfect weapon to combat the troubling case of genetic diseases.

As more research began to be conducted on this revolutionary piece of technology, the potential applications of CRISPR emerged closer to reality from an indefinite hope for the future. The first focus of research is in improving CRISPR's effectiveness and efficiency for lab or clinical purposes. The advancements sought to improve CRISPR's detectability (of the regions), attachability (binding to the site), accuracy (in performing the gene fix), and leaving no side effects, especially as the technology might be introduced to *in vivo*, which is when CRISPR performs its job in the body. One of the significant enhancements



Figure 1: March 14, 2016 American biochemist Jennifer A. Doudna, left, and the French microbiologist Emmanuelle Charpentier, right.

at its roots, CRISPR technology has shown positive outcomes in directly knocking out the oncogenes, correcting mutations in tumor suppressor genes, and enhancing the efficacy of T-cell therapies (Davis & Yeddula, 2024), and they are already on phase one clinical trials. The studies also show that CRISPR can assist in boosting immunity to cancer, or inactivating oncogenes mutants when they disturb the normal cell cycle. More generally, regenerative medicine using CRISPR is also gaining success thanks to the more advanced modern editing strategies, which eliminated the requirement of immunosuppressive drugs as the CRISPR medicines had become more immune-tolerant.

Conclusion

As modern medical technology development empowers us with greater tools in treating diseases, genetic illnesses still pose a prominent concern to humans. Currently, CRISPR—a frontline, revolutionary gene-editing tool—stands as the most promising candidate for treating genetic diseases and holds immense potential for future improvements and medical breakthroughs. With efforts to further the technological advancement and initiate clinical application, CRISPR can play a tremendous role in treating some of the most troublesome diseases in the near future— or even in the present day. However, like other novel technologies, the ethical implications must be carefully examined to maximize benefits and minimize risks. The future of CRISPR will depend on the continued progress of scientific research, responsible administration, and the global community’s willingness to cooperate if the mankind is to harness this powerful tool for the benefit of all. Nevertheless, this cutting-edge technology will ultimately be in the limelight of bio-scientific research in the following years and will undoubtedly contribute invaluable findings and assistance to the science community, medicine industry,

and society

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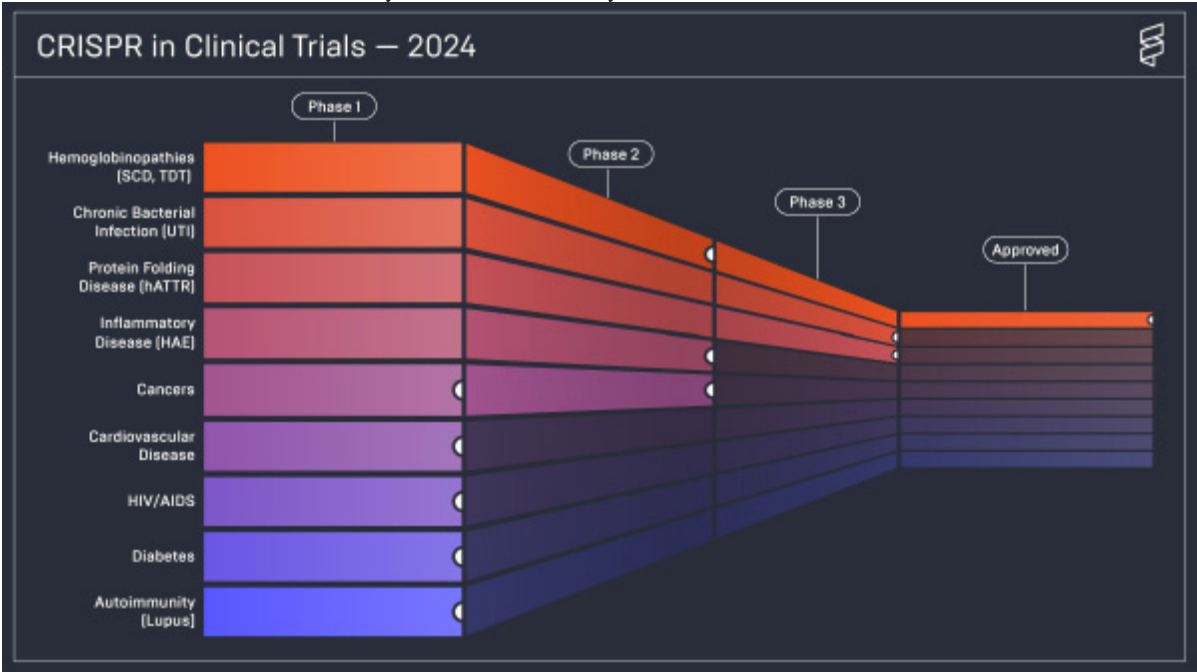


Figure 3: CRISPR in Clinical Trials as of 2024

Hypersonic Flight:

Current Challenges and Future Applications

Article by **Brady Kim '26**

Hypersonic speeds categorize the movement of an object travelling more than five times faster than the speed of sound. Such high speeds are typically interpreted using Mach numbers, which are quantities measuring the ratio between an object's velocity and the local speed of sound. So, the speed of sound in air is Mach 1, about 767 miles per hour, while hypersonic speeds are greater than Mach 5, almost 4000 miles per hour. Using the definition of hypersonic speed, hypersonic flight is then defined as flight through Earth's atmosphere at speeds greater than Mach 5. While the future applications for hypersonic flight are numerous, such as commercial flight and military technology, current major engineering challenges like high thermal loads and reliable propulsion systems stand in the way of its development.

As an aircraft reaches speeds greater than Mach 5, intense air friction generates an extreme amount of heat which hypersonic aircraft must be able to withstand. Certain areas of a hypersonic aircraft may experience temperatures up to 2000 degrees Celsius, or about 3632 degrees Fahrenheit. Consequently, a challenge still at the forefront of the field is the development of a light material that can withstand these temperatures without compromising durability. Carbon-carbon, the material used in rocket nozzles, prevents spacecraft from burning up during re-entry but inevitably begins to ablate. Therefore, it doesn't quite meet the rigorous demands of hypersonic vehicles, which must contain materials that won't erode under heat and consequently hinder maneuverability.

Another current obstacle facing hypersonic flight is the lack of an efficient and reliable propulsion system that can accelerate a vehicle to hypersonic speeds. The ramjet and scramjet are two engines capable of achieving the sufficiently high thrust to weight ratios necessary for hypersonic flight. Unlike a traditional jet engine, the air-breathing ramjet and scramjet engines do not have any moving parts in them. When attached to a moving aircraft, these engines rely on the forward motion and speed of the aircraft to compress incoming air and mix it with fuel, generating thrust through a combustion reaction. The major problem with these engines, however, is that they cannot produce any thrust when stationary and instead require a flying start. Therefore, engineers are still working to develop a propulsion system that can accelerate from rest to sustained hypersonic speeds, have a low thrust to weight ratio, and remain lightweight but resistant to the extreme conditions of Mach 5 and beyond.

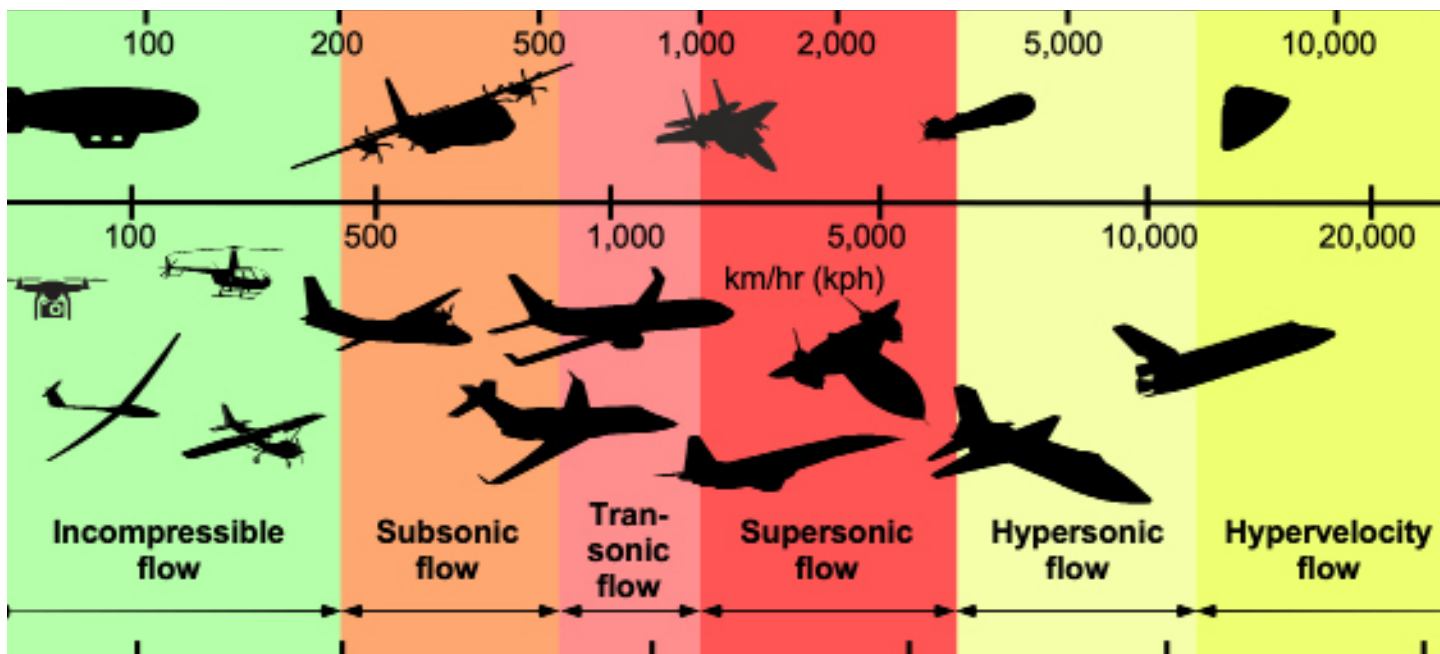


Figure 1: Representation of Airspeed and Aerospace Flight Vehicles

Even with the current challenges faced with its development, the race to achieve stable hypersonic flight has numerous future applications in the military realm. In fact, hypersonic weapons have provoked a new arms race between major military powers like the U.S. and Russia, who have been researching the development of hypersonic missiles capable of traversing long distances while maintaining maneuverability. Though ballistic missiles that travel at hypersonic speeds exist today, they are unable to change course once launched. That technology is used rather in cruise missiles, who's next developmental step is matching the speed of their ballistic counterparts.

Outside of military purposes, hypersonic flight is also attracting attention for its applications commercially, namely the prospect of ultra-fast passenger planes. A few startup companies have already set out to meet this demand. One popular startup is the Switzerland-based company Destinus, which is proposing a hydrogen-powered hypersonic passenger jet. Their plane uses a combination between a turbojet and ramjet engine to reach hypersonic speeds. Predicted to be in service before 2040, these planes will be able to connect passengers from cities such as London and New York in about an hour and a half. To put this into perspective, a flight on a normal passenger jetliner from London to New York takes anywhere from seven to eight hours. Although concerns about passenger safety and other challenges currently exist, hypersonic passenger planes would be a generational breakthrough for the aviation industry, and many businesses are competing for who will solve the problem first.

In conclusion, the pursuit of hypersonic flight, defined as speeds exceeding Mach 5, presents a revolutionary frontier in aviation with promising applications for the future in both military and commercial flight. Despite this exciting potential, current engineering challenges still stand in the way of achieving success in this field. High thermal loads, stemming from intense air friction during hypersonic travel, demand advanced materials capable of withstanding extreme temperatures. Additionally, the development of propulsion systems capable of accelerating from rest remains an issue. But despite the complicated engineering challenges that stand in the way of hypersonic flight, many businesses and countries are invested in what could be the next great marvel of aviation.

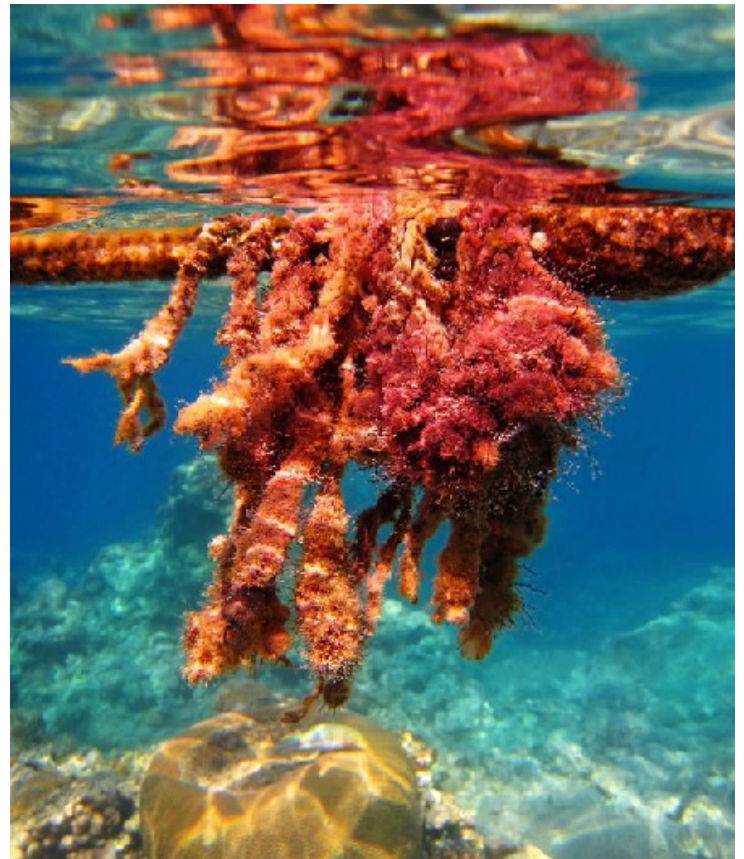
The Prospect of Mass Extinction

Article by **Julian Zhang '26**

Astronomer and science writer Carl Sagan once stated, “Extinction is the rule. Survival is the exception” (Sagan, 2006). Sagan was undoubtedly correct: extinction is a natural part of life. In fact, approximately 98% of all organisms existent in our planet’s history are extinct. Due to the fact that extinct species are generally replaced, life is able to persist. However, in the event that the extinction of a large number of species far exceeds the rate at which they are replaced, a mass extinction crisis ensues. Mass extinction is most often defined by scientists as the loss of three-quarters of all species on Earth within the short geological time period of 2.8 million years (Saltré & Bradshaw, 2019). There have been five mass extinctions, including the Ordovician, Devonian, Permian, Triassic-Jurassic, and the Cretaceous-Tertiary mass extinction. The prospect of a current sixth is also plausible on account of recent drastic weather and ecological changes.

In an effort to examine the present circumstances challenging biodiversity, it is vital to analyze previous mass extinctions. The first of which is the Ordovician mass extinction. This extinction occurred during the Ordovician Period of the Paleozoic Era, around 440 million years ago, wiping out nearly 85% of all species on Earth. During this time, life was in its emergent stages. The first-known life forms had begun to appear 3.6 billion years prior, but by this period, larger aquatic organisms, as well as land species, were coming into existence. The causation of this mass extinction is often attributed to a continental shift and climate change. This ultimately happened in two phases. It started with an ice age that took over the entirety of the planet. Sea levels thereafter dropped, and species, especially those living on land, were unable to adapt quickly enough to sustain life. Then, the glaciation ended abruptly, and sea levels rose so rapidly that those who survived the first episode died out. While all the major animal groups, including trilobites, brachiopods, corals, crinoids, and graptolites, survived, many integral members of each were lost. Trilobites and graptolites almost faced complete extinction (“End-Ordovician extinction,” n.d.).

The second mass extinction was the Devonian mass extinction of the Devonian Period of the Paleozoic Era, relatively 375 million years ago. Of all living species, 80% were eliminated. By the Devonian Period, living species such as ammonites, starfish, corals, crinoid stems, armored fish, sharks, early bony fish, and early amphibians had evolved from the remnants of the Ordovician mass extinction (“The structure of geologic time,” n.d.). However, just as the climate had stabilized and life on Earth was flourishing, the bulk of species were expunged. There are several hypotheses attempting to explain this mass extinction. The first wave, which dealt a major blow to aquatic life, may have been caused by the sudden colonization of land. Many aquatic plants had acclimated to land, leaving fewer autotrophs or producers to create oxygen for the totality of sea life. As a result, the oceans encountered widespread death. This move of aquatic plant life to land also conceivably removed significant quantities of carbon dioxide from the atmosphere. The scarcity of this gas likely resulted in extremely low temperatures. Thus, land species failed to adjust accordingly, going extinct. The second wave



is not as straightforward. It may have involved volcanic eruptions and meteor strikes, but the exact cause is unknown.

Following the first two mass extinctions, the third mass extinction was the Permian mass extinction, which took place during the last period of the Paleozoic Era, the Permian Period, about 250 million years ago. This is the largest known mass extinction in the history of Earth, with an estimated 96% of all species lost. Truly distinct from the previous mass extinctions, this mass extinction saw the destruction of life to an extent and at a pace unseen before then. It is no surprise that the event has been dubbed “The Great Dying.” For context, the Permian Period marked the collision and amalgamation of the two great continents of the Paleozoic Era, Gondwana and Euramerica, to form the supercontinent, Pangea and the Panthalassic Ocean. While life on Pangea is sufficiently documented, there is little known about this huge ocean.



Figure 1: Fossilized Coelacanth Fish

What is known is that the fossils found in shallower coastal waters demonstrate that reefs were diverse ecosystems with an abundance of different sponge and coral species. Spiny and lobe-finned fish were replaced by the nascent true bony fish, while sharks and rays continued to thrive. Concurrently, on land, massive swamp forests of carboniferous were drying out. The constituents of this environment were identified by two primary classifications: Synapsids and Sauropsids. Synapsids had skulls with a single temporal opening and have been speculated to be the origins of mammal life. Sauropsids had two skull openings and were the ancestors of reptiles and soon-to-be dinosaurs (Bagley, 2014).

It is still a mystery as to what provoked the Permian mass extinction. Some scientists believe a chain of events of volcanic activity paired with asteroid impacts must have unfolded. This could have brought about lethal amounts of methane and basalt in

This was a combination of a succession of smaller extinction events. Over the course of this progression, over half of Earth's species perished. The source of this extinction can be traced back to volcanic activity with basalt flooding. The gases produced by eruptions also created climate change issues and altered sea levels as well as ocean pH levels. The final and most famous mass extinction was the Cretaceous-Tertiary Mass Extinction. Dating back 65 million years, this became the dividing line between the Cretaceous Period, the last period of the Mesozoic Era, and the Tertiary Period, the first of the Cenozoic Era. Excluding dinosaurs, who were thoroughly erased, up to 75% of all species, including free-swimming mollusks and inoceramidae, became extinct. The only surviving lines of archosaur lineage are those that led to modern birds and crocodilians (“K-T extinction,” 2020). It is common knowledge that the extinction was the outcome of a powerful asteroid impact. Space rocks hit Earth and shot debris up into the air, prompting an “impact winter,” which irreversibly modified the Earth's climate. Scientists have studied craters, most notably the Chicxulub Crater, off the Yucatán Peninsula in the Gulf of Mexico and have confirmed through findings the suspected cause of the K-T mass extinction (Parks, 2021).

Knowing the conditions that have preceded mass extinctions, a sixth one is far from outlandish. The exploitation and industrialization of the planet by humans have accelerated processes of global warming (Scoville, 2020). Yet, does this constitute a mass extinction? Could the mammoth, smilodon, dodo bird, thylacine, and quagga all be the initial signs of a mass extinction?



Figure 2: Chicxulub Crater off the Yucatán Peninsula

Humans have already transformed over 70% of land surfaces and are making use of 75% of freshwater resources. Agriculture is a leading cause of soil degradation, deforestation, and pollution, driving innumerable native species from their habitats. Hunting practices and overfishing only have adversely brought many species to near extinction. Selective removal of species by humans has manufactured trophic ecological cascades. Invasive species, many of which are introduced by humans, are posing undeniable threats worldwide. The embedded interwovenness of the planet's life forms is being distorted and in danger of collapse. Never before in the history of our planet has one single species been culpable for the magnitude of destruction visible in our world today. It is for these reasons and examples of disregard that mass extinction is a practical concern.

In closing, it is imperative that we inspect Earth's history to evade the boundless consequences of a sixth mass extinction. A shift in our attitude, and particularly our action toward the risks of climate change is needed. We have been informed of the dire situation concerning our environment, and now it is up to us how we proceed.

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Ideonella Sakaiensis

Article by **Julian Zhang** '26

INTRODUCTION

In the genus *Ideonella* and family Comamonadaceae, a bacterium *Ideonella sakaiensis* can break down and consume PET plastic as its only carbon and energy source. The bacteria was first found in a plastic bottle recycling plant in Sakai Japan. (Yoshida et al., 2016)

DISCOVERY

Researchers headed by Kohei Oda and Kenji Miyamoto of Kyoto Institute of Technology and Keio University collected a sample of PET-contaminated sand near a plastic bottle recycling facility in Japan in 2016 to identify '*Ideonella sakaiensis*.' Microorganisms including protozoa and yeast-like cells were found in the sand sample where the bacteria was isolated. After early degradation and assimilation by '*Ideonella sakaiensis*', the whole microbial community was demonstrated to mineralize 75% of the degraded PET into carbon dioxide. (Yoshida et al., 2016).

WORKING OF IDEONELLA SAKAIENSIS

For hundreds of years, the plastic bottles we toss away now will be around. As a result, plastic pollution, which has a devastating impact on marine life, is becoming more and more of an issue. A new strain of bacteria that can devour the plastic used to produce bottles has just been identified and has been tweaked to make it function quicker. Bacteria might be a valuable tool in the fight against plastic pollution, even if the results aren't as dramatic as they could be. (Hopewell, Dvorak, & Kosior, 2009).

Polymers are lengthy, repeating chains of chemicals that do not dissolve in water. Plastics are complicated polymers. Plastic decomposes slowly due to these chains' tensile strength, making it very durable. A closed-loop recycling system for plastics may be created if they could be broken down into smaller, soluble chemical components. *Ideonella sakaiensis* 201-F6 was shown to be able to break down polyethylene terephthalate, the plastic used to create single-use drinks bottles, in a bottle recycling factory in Japan in 2016. (PET).

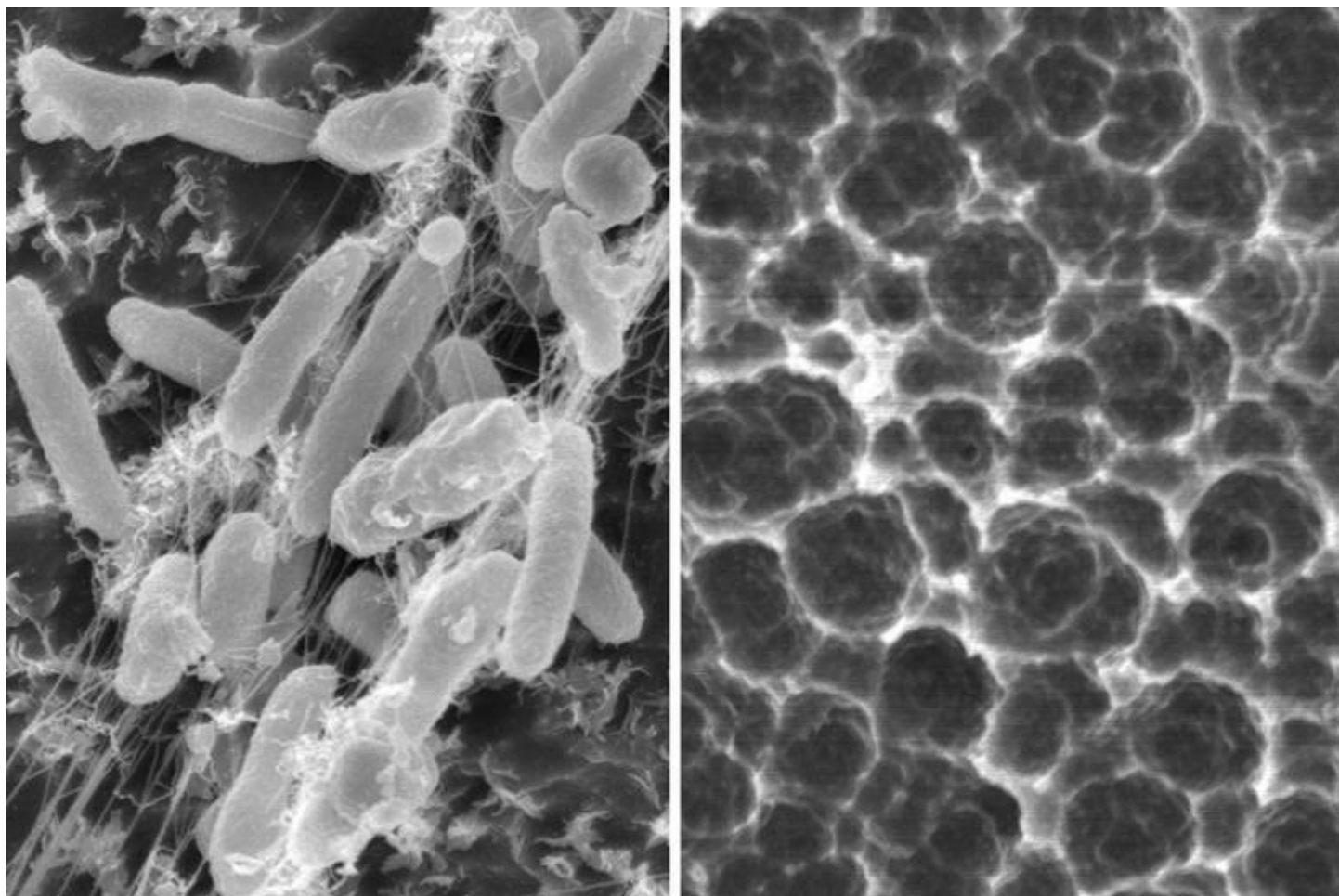


Figure 1: Microscopic view of *Ideonella Sakaiensis*

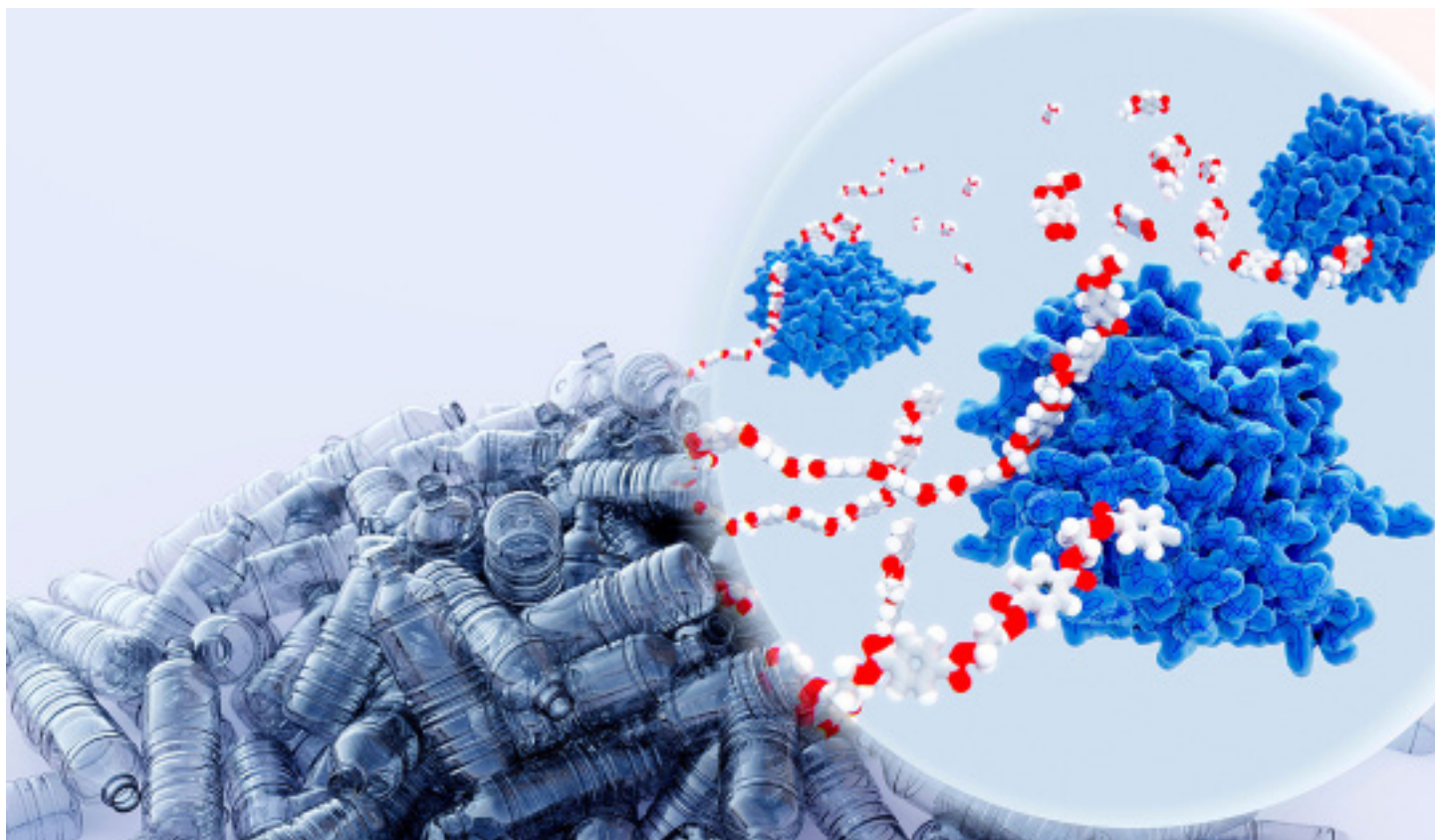


Figure 2: *Ideonella Sakaiensis* in Single Use Drinking Bottles

WHAT IS PETASE?

Known as PETase, PET hydrolase is a newly discovered enzyme that has been proven to break down PET, or polyethylene terephthalate. ($C_{10}H_8O_4$)_n. In addition to being used for single-use plastic bottles, straws, film, packaging 'peanuts', and numerous fibers in garments, PET is a widespread form of plastic. Although PET may be recycled up to ten times (in the case of plastic bottles) and once or twice (in the case of polyester clothes) for reuse, it is a substantial contributor to waste plastic and plastic in the ocean, even though it is recyclable. Although PET bottles may be recycled, many people don't bother and just discard them in the trash, as seen by the pictures of plastic bottles floating in the ocean below. (Roth et al., 2014).

Because it hasn't biodegraded for 450 years and has the potential to ruin habitats, trap and poison animals, clog parks, seas, and cities with litter, as well as being toxic to produce, PET is one of the most environmentally damaging plastics on the market today. Due to the increasing demand, production rates are incredibly high, resulting in many more new PET products being introduced into the environment. A unique enzyme that can break down and dispose of waste PET is very beneficial since it reduces landfill space and eliminates the massive volumes of PET that are now accumulating in landfills.

For the first time, PETase has been detected in certain fungal organisms, including *Pestalotiopsis microspore*, which was discovered by Yale University in 2012. (Roth et al., 2014). Some microorganisms contain it, which expands its range of uses in nature. It is possible that 'super' mushrooms are the answer to preserving the earth.

HOW DOES IT WORK?

After administering bacteria or fungus harboring the PETase enzyme to the PET plastic, they release the enzyme, which enables the polymers to bind to the active site, permitting the process. The enzyme breaks PET ester bonds during the process. The PETase remains intact, but the PET has been broken down into MHET and BHET at the conclusion of the process. However, BHET and MHET may both be broken down into smaller molecules. TPA, or terephthalic acid, and EG, or ethylene glycol, are produced as monomers when an enzyme in the fungus or bacterium breaks down the MHET. Fungi will use BHET, TPA, and EG as food after digesting the reaction's end products (the carbon is the part that is nutritious to them) (Müller, Schrader, Profe, Dresler, & Deckwer, 2005).

CONCLUSION

Plastic deterioration may be helped by the discovery of *Ideonella sakaiensis*. Until *Fusarium solani* was discovered, the only organisms that could reliably break down PET as a carbon and energy source were a tiny number of bacteria and fungi. Discussion over PET biodegradation was reignited with the discovery of *I. sakaiensis*. (Yoshida et al., 2016).

Wild-type bacteria can colonize and break down a 0.2 mm-thick coating of low-crystallinity (soft) PET in about six weeks, and the PETase enzyme responsible for this degradation is about 30 times slower than low-crystallinity (soft) PET (180 weeks or more than 3 years). *I. sakaiensis* PETase enzyme may be used in recycling systems, although genetic modification of the enzyme may be necessary due to the highly crystalline nature of many PET products (e.g., plastic bottles). (Müller et al., 2005) (Yoshida et al., 2016).

A combination of the MHETase enzyme and the PETase enzyme might be employed in recycling or bioremediation applications. Ethylene glycol and terephthalic acid are formed as a result of the PETase's breakdown of the MHET generated by the enzyme. (Yoshida et al., 2016) *I. sakaiensis* or other bacteria may further biodegrade these two chemicals into carbon dioxide, or they can be purified and employed in an industrial recycling plant setting to make new PET. (Yoshida et al., 2016) (Al-Sabagh, Yehia, Eshaq, Rabie, & ElMetwally, 2016).

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MTWSI-Net: Towards Improved Multi-Task Whole Slide Image Classification with Contrastive Learning

Article by **Sean Hwang '26**

ABSTRACT

Pathology is a digital technology for the capture and analysis of high-resolution Whole Slide Images (WSIs). WSI entails scanning glass pathology slides, typically containing tissue samples, into a digital format. This facilitates comprehensive digital viewing, analysis, and interpretation by pathologists. Despite the undeniable utility of this method, the inherent time-consuming and labor-intensive nature of traditional pathology image analysis, which is heavily reliant on expert pathologists, is well-known. Recent years have seen a surge in research aiming to address these challenges through the development of automated systems using machine learning approaches. While promising, such systems often exhibit bias towards specific datasets and struggle to transition effectively to real-world scenarios. For this reason, there is a need to establish a uniform machine learning training approach for generating more robust and consistent results. In this paper, I introduce a contrastive learning-based multi-task whole slide image classification system. The proposed system excels at extracting consistently reliable features for identical cancer categories, thereby enhancing accuracy in downstream tasks. Through extensive experiments, the results demonstrate that the proposed system outperforms pre-existing state-of-the-art machine learning models. I expect that the proposed system can significantly contribute to pathologists by offering valuable cancer screening capabilities in WSIs.

1. Introduction

Pathology has witnessed a revolutionary shift with the adoption of Whole Slide Imaging (WSI). This innovative technology involves the digitization of traditional glass pathology slides which enables pathologists to engage in comprehensive digital analysis of tissue samples. Despite the benefits of WSIs, the traditional pathology process is a time-consuming and labor-intensive endeavor, as pathologists manually analyze WSIs.

This reliance on subjective visual inspection poses challenges which hinders the efficiency of pathology workflows. In response to the inherent limitations of traditional methods, recent years have seen the emergence of machine learning-based techniques designed to automate and expedite pathology image analysis. These approaches hold the promise of alleviating the burdensome nature of manual assessments and improving diagnostic accuracy. However, a critical challenge emerges in the application of these machine learning models to real-world scenarios. Many existing techniques exhibit a propensity to be biased towards specific training datasets. This limitation poses a significant barrier to the seamless integration of machine learning solutions into the real-world. In this research paper, I propose a solution to tackle the bias issue in machine learning-based pathology image analysis. I introduce a novel contrastive learning-based multi-task WSI analysis system. The proposed system aims to not only enhance the efficiency and accuracy of pathology image analysis but also ensure its applicability in diverse and real-world clinical settings.

The subsequent chapters are structured as follows: Chapter 2 provides background knowledge essential for a comprehensive understanding of the proposed approach. In Chapter 3, every detail of the proposed system is elaborated upon, with comprehensive experimental results presented and analyzed in Chapter 4. The concluding insights are summarized in Chapter 5.

2. Related Work

2.1 Image Classification

Image classification is a task in computer vision and machine learning which aims to train a model to categorize images or objects into predefined classes or labels. The goal is to enable the system to automatically recognize and assign a label to a given image based on its visual content. Convolutional neural networks are commonly used for image classification due to their ability to automatically learn hierarchical features from images. They consist of convolutional layers that capture spatial hierarchies and pooling layers for feature reduction.

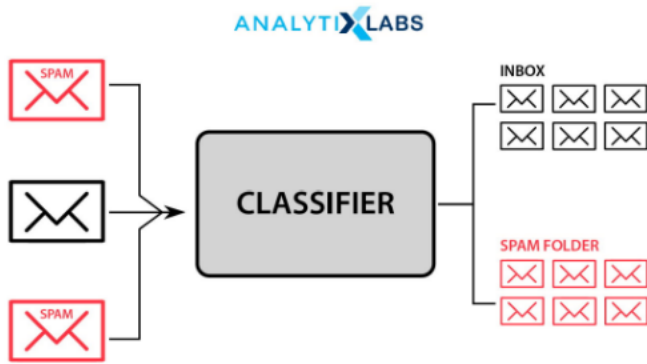


Figure 1. Example of object classification (Bansal 2023)

Due to the success of convolutional neural network-based image classification, its application in analyzing Whole Slide Images (WSI) in pathology has experienced rapid growth. These models effectively learn to discern visual patterns indicative of specific cancer types within WSI, yielding promising results for the detection of cancer cells across diverse human organs. Further details on this topic will be elaborated in the subsequent section, Chapter 2.1.

2.1 Whole Slide Images

Whole Slide Images (WSIs), also known as digital slides, refer to high-resolution digital representations of entire pathology slides. Traditional pathology involves the examination of tissue samples under a microscope, but with WSI, the entire slide is scanned and digitized. This digital transformation allows pathologists to view and analyze the entire specimen at varying magnifications on a computer screen, offering several advantages over conventional microscopy. Similarly, Sun et al. presented a cancer type classification system for the liver using a similar approach (Sun et al., 2019). Kuntz et al. developed a machine learning model specifically for the classification and prognostication of gastrointestinal cancer (Kuntz et al., 2021).

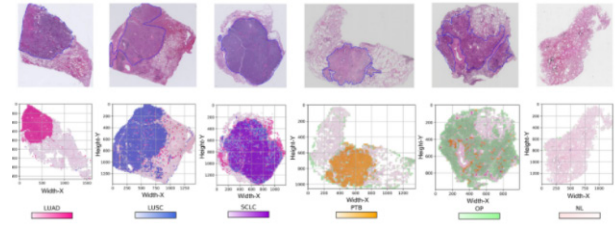


Figure 2. Example of WSI classification (Yang et al. 2021)

While these methods have demonstrated promising results, a notable limitation lies in their pronounced bias toward specific datasets, rendering them less applicable to real-world scenarios. Therefore, there is a need to study and develop a uniform training approach to enhance the generalizability of trained models. In this research, to solve this problem, I introduce a novel contrastive learning-based cancer type classification system. The detailed information of the proposed approach will be explained in Chapter 3

Therefore, there is a need to study and develop a uniform training approach to enhance the generalizability of trained models. In this research, to solve this problem, I introduce a novel contrastive learning-based cancer type classification system. The detailed information of the proposed approach will be explained in Chapter 3.

3. Proposed Method

The proposed method comprises two distinct training phases. The initial phase focuses on representation learning which aims to train the feature extraction process to extract consistent features from diverse cancer images. In the second phase, this trained feature extractor is leveraged through transfer learning to enhance the efficiency and accuracy of downstream tasks. Both representation learning and transfer learning phases are illustrated in Figure 3 and Figure 4.

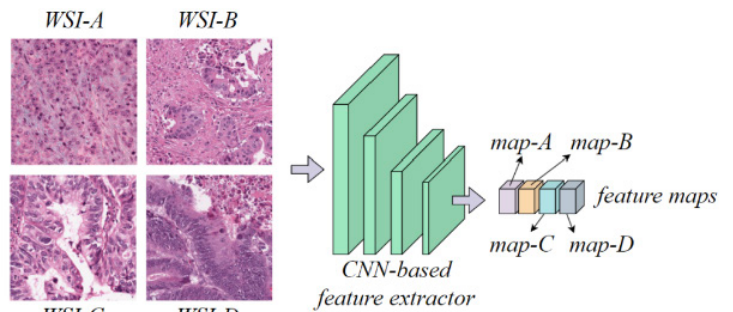


Figure 3. Architecture of the proposed representation learning approach.

The convolutional neural network-based feature extractor processes the input of four pairs of Whole Slide Images (WSIs). These images are transformed into four distinct feature maps labeled as map-a, map-b, map-c, and map-d. The objective is to maximize the similarity between two feature maps derived from WSIs belonging to the same cancer category. Despite potential variations in pixel-level visual patterns, the latent features are expected to exhibit similarity, given that they pertain to identical cancer types. To accomplish this, I utilize the cosine similarity function to quantify the similarity between each pair of feature maps and calculate the corresponding loss value. The step-by-step process is explained in Equations 1-3.

$$S_{(\alpha, \beta)} = \frac{map_{\alpha} \cdot map_{\beta}}{|map_{\alpha}| \times |map_{\beta}|}$$

Equation 1: Cosine similarity function

In the Equation 1, $S(a,b)$ denotes the similarity index or score of two feature maps map-a, and map-b. The similarity score ranges from 0 to 1. A score of 0 signifies that two feature maps are diametrically opposed, whereas a score of 1 indicates that the two feature maps are identical. Three total score values are computed from the four feature maps. These scores are fed to the softmax function to generate probabilities, as explained in Equation 2.

$$P_{(\alpha, \beta)} = \frac{e^{S_{(\alpha, \beta)}}}{e^{S_{(\alpha, \beta)}} + e^{S_{(\alpha, c)}} + e^{S_{(a, d)}}$$

Equation 2: Softmax function

In Equation 2, $P(a, b)$ represents the converted probability of the similarity score $S(a, b)$. Among the probabilities derived from all three score values, the probability associated with the score calculated from the same category should be maximized. To quantify the disparity between the prediction and ground truth, I employ the cross-entropy loss function commonly utilized in various classification tasks. The cross-entropy loss function is detailed in Equation 3.

$$L = -\log_e P$$

Equation 3: Cross-entropy loss function

Here, P denotes the predicted probability, and L denotes the calculated loss value. Throughout the training process, the model is optimized to minimize the loss value, thereby refining the parameters of the feature extractor to extract more consistent features from inputs of the same category. Following training, the pre-trained feature extractor is employed in the downstream task.

The MSI vs. MSS Classification dataset is sourced from histological images of colorectal cancer and gastric cancer patients. The dataset comprises 411,890 unique image patches. Microsatellites, also known as short tandem repeats or simple sequence repeats, are repetitive sequences of DNA scattered throughout the genome. They consist of short sequences of nucleotides repeated in tandem, and their stability is crucial for maintaining genomic integrity. MS) and MSS refer to conditions where there is a deviation from the normal stability of these repetitive sequences.

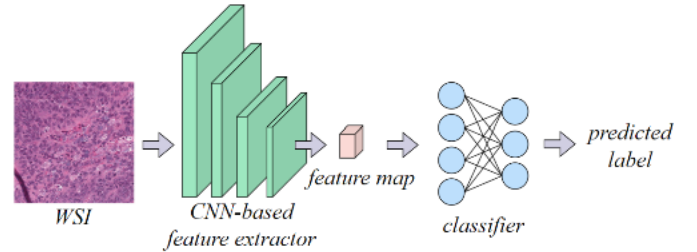


Figure 4. Architecture of the proposed transfer learning approach

Figure 4 illustrates the architecture of the proposed transfer learning approach. The pre-trained feature extractor receives a single WSI as input and generates a feature map, which is then input into the subsequent cancer type classifier. The classifier outputs the predicted cancer type. Instead of training this classification network from randomly initialized weights, I employ transfer learning, where the pre-trained feature extractor serves as the starting point for training weights. This training approach facilitates faster training and yields more accurate results. Additionally, the cross-entropy loss function is applied in training the model during transfer learning, with the mathematical equation being identical to Equation 3.

4. Experimental Results

4.1 Dataset and Evaluation Metrics

To train and evaluate the performance of the proposed model, I employed three distinct Whole Slide Image (WSI) classification datasets, including the Microsatellite Instable (MSI) vs. Microsatellite Stable (MSS) dataset from Nicolas (2019), the Metastatic Tissue dataset from Kaggle (2020), and the Breast Cancer dataset from Mooney (2017).

The Metastatic Tissue dataset utilized in this study comprises a total of 327,680 WSIs. The dataset is curated from histopathologic scans of lymph node sections. The primary focus of this dataset is the annotation of images with binary labels indicating the presence or absence of metastatic tissue.

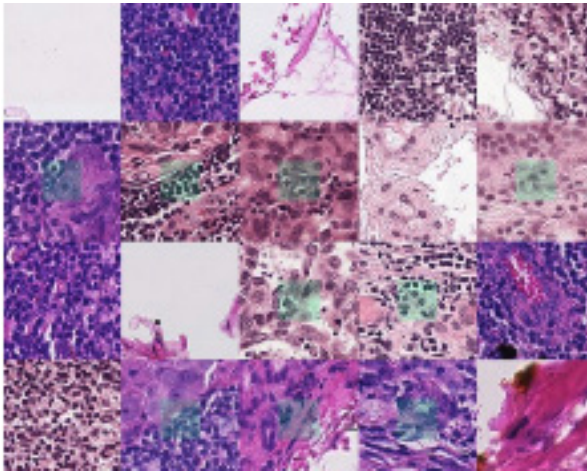


Figure 5. Metastatic Tissue dataset (Nicolas 2019)

The Breast Cancer dataset consists of 162 WSIs, each scanned at a magnification of 40x. A total of 277,524 patches were extracted from these whole mount slides. These patches are categorized into two classes: Invasive Ductal Carcinoma (IDC) negative (198,738 patches) and IDC positive (78,786 patches). IDC is the most common type of breast cancer, accounting for approximately 70-80% of all breast cancer diagnoses. It originates in the milk ducts of the breast but has the potential to invade surrounding tissues in the breast.

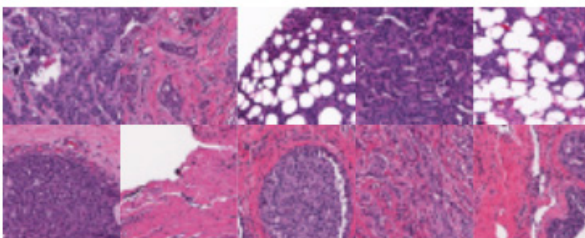


Figure 6. Breast Cancer dataset (Mooney 2017)

The MSI vs. MSS Classification dataset is sourced from histological images of colorectal cancer and gastric cancer patients. The dataset comprises 411,890 unique image patches. Microsatellites, also known as short tandem repeats or simple sequence repeats, are repetitive sequences of DNA scattered throughout the genome. They consist of short sequences of nucleotides repeated in tandem, and their stability is crucial for maintaining genomic integrity. MS) and MSS refer to conditions where there is a deviation from the normal stability of these repetitive sequences.

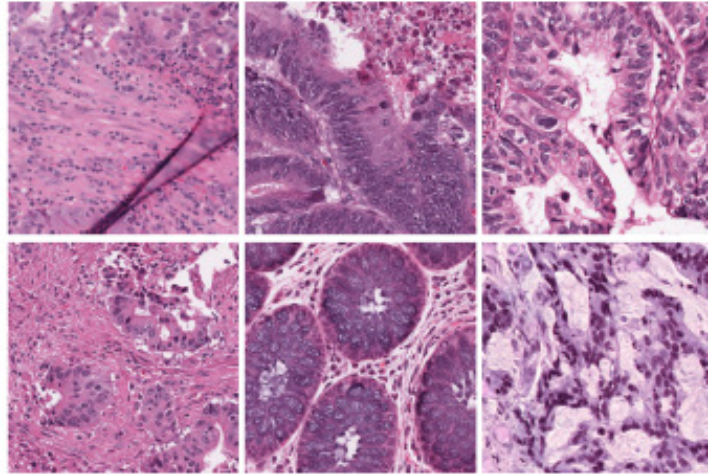


Figure 7. MSI vs. MSS dataset (Nicolas 2019)

To assess the effectiveness of the proposed method, I quantified its performance using four widely employed evaluation metrics: accuracy, recall, precision, and F1-score, as commonly applied in various classification tasks (Yacoubi et al., 2020).

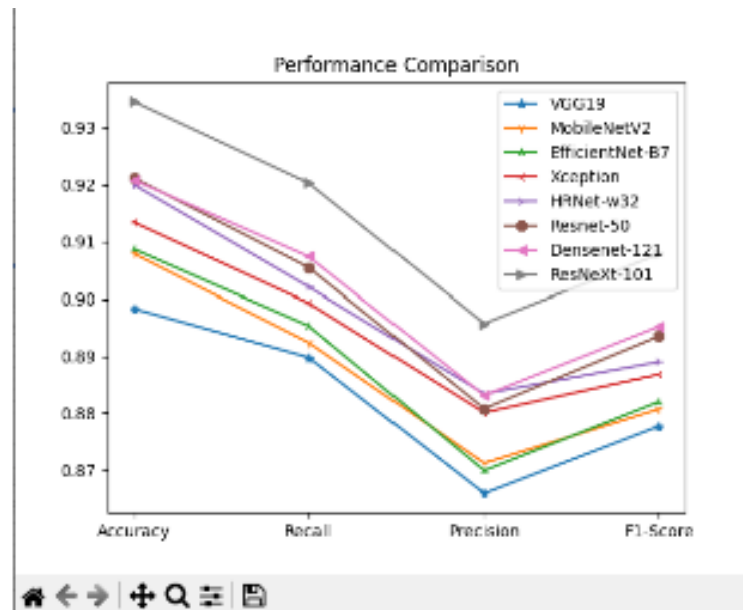


Figure 8. Evaluation results on various network architectures (MSI vs. MSS dataset)

Table 1. Evaluation results on various network architectures (MSI vs. MSS dataset)

	Accuracy	Recall	Precision	F1-Score
VGG19	0.8983 (± 0.0013)	0.8898 (± 0.0011)	0.8659 (± 0.0015)	0.8777 (± 0.0014)
MobileNetV2	0.9079 (± 0.0007)	0.8924 (± 0.0007)	0.8712 (± 0.0008)	0.8807 (± 0.0013)
EfficientNet-B7	0.9087 (± 0.0010)	0.8953 (± 0.0008)	0.8699 (± 0.0009)	0.8820 (± 0.0011)
Xception	0.9134 (± 0.0012)	0.8993 (± 0.0015)	0.8801 (± 0.0010)	0.8868 (± 0.0012)
HRNet-w32	0.9200 (± 0.0006)	0.9021 (± 0.0011)	0.8834 (± 0.0015)	0.8890 (± 0.0009)
Resnet-50	0.9212 (± 0.0012)	0.9055 (± 0.0015)	0.8808 (± 0.0016)	0.8935 (± 0.0014)
Densenet-121	0.9208 (± 0.0008)	0.9074 (± 0.0011)	0.8831 (± 0.0012)	0.8952 (± 0.0011)
ResNeXt-101	0.9346 (± 0.0005)	0.9203 (± 0.0008)	0.8957 (± 0.0008)	0.9078 (± 0.0010)

Table 1 and Figure 8 provide a comprehensive summary of the evaluation results obtained across various network architectures using the MSI vs. MSS dataset. In the experimentation phase, I trained multiple network architectures including VGG19 (Simonyan et al. 2014), MobileNetV2 (Sandler et al. 2018), EfficientNet-B7 (Tan et al. 2019), Xception (Fran et al. 2017), HRNet-w32 (Wang et al. 2020), Resnet-50 (He et al. 2016), Densenet-121 (Huang et al. 2017), and ResNeXt-101 (Xie et al. 2017), leveraging the proposed representation learning approach.

VGG19, MobileNetV2, and EfficientNet-B7 exhibited relatively inaccurate results, possibly due to their shallower network depth. In contrast, both HRNet-32 and ResNet-50, equipped with deeper convolutional layers, demonstrated significantly improved efficacy. Notably, all evaluation results (accuracy) surpassed the 89% threshold, marking a remarkable achievement. The effectiveness of the proposed representation learning is elaborated in detail in Chapter 4.2.3.

Figure 9 showcases the confusion matrix and the receiver operating characteristic (ROC) curve for the methods proposed in the MSI vs. MSS classification dataset. A close look at the diagonal elements of the confusion matrix offers compelling evidence of the stability and consistency realized by our proposed approach.

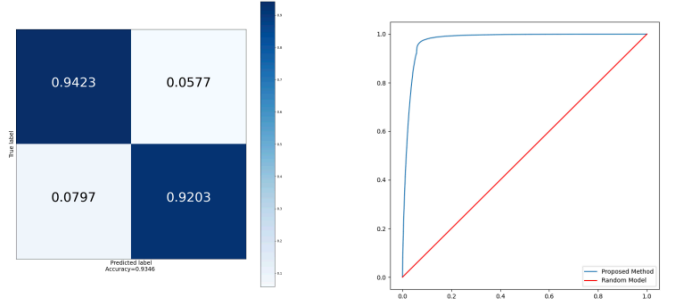


Figure 9. Confusion matrix and ROC curve (MSI vs. MSS dataset)

Furthermore, the ROC curve's pronounce near-rectangular contour in the upper-left quadrant suggests that the method has outstanding results.

4.2.2 Metastatic Tissue dataset

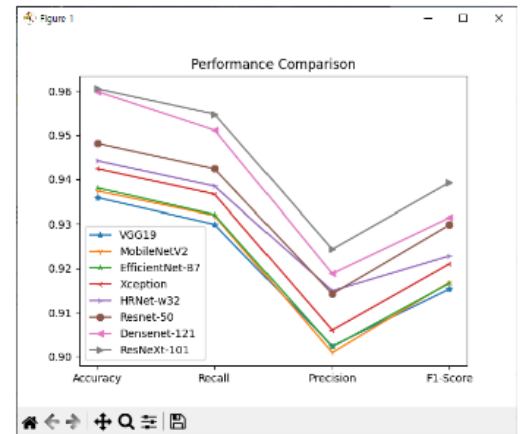


Figure 10. Evaluation results on various network architectures (Metastatic Tissue dataset)

Table 2. Evaluation results on various network architectures (Metastatic Tissue dataset)

	Accuracy	Recall	Precision	F1-Score
VGG19	0.9359 (± 0.0014)	0.9299 (± 0.0013)	0.9024 (± 0.0015)	0.9153 (± 0.0011)
MobileNetV2	0.9374 (± 0.0013)	0.9319 (± 0.0011)	0.9009 (± 0.0012)	0.9168 (± 0.0010)
EfficientNet-B7	0.9381 (± 0.0007)	0.9321 (± 0.0009)	0.9022 (± 0.0007)	0.9166 (± 0.0006)
Xception	0.9424 (± 0.0006)	0.9369 (± 0.0008)	0.9060 (± 0.0011)	0.9210 (± 0.0007)
HRNet-w32	0.9442 (± 0.0006)	0.9385 (± 0.0007)	0.9149 (± 0.0009)	0.9228 (± 0.0011)
Resnet-50	0.9481 (± 0.0012)	0.9424 (± 0.0010)	0.9142 (± 0.0013)	0.9298 (± 0.0010)
Densenet-121	0.9599 (± 0.0011)	0.9512 (± 0.0013)	0.9512 (± 0.0013)	0.9314 (± 0.0011)
ResNeXt-101	0.9605 (± 0.0010)	0.9548 (± 0.0009)	0.9243 (± 0.0013)	0.9393 (± 0.0014)

In parallel with the initial experiment, I replicated the study on the Metastatic Tissue dataset to assess the applicability of the proposed approach to a distinct dataset. As depicted in Figures 5 and 7, the pixel distributions of the two datasets exhibit notable differences. The results, outlined in Table 2 and illustrated in Figure 10, reveal that all four evaluation metrics consistently achieve outstanding performance, surpassing the 90% threshold. This compelling outcome demonstrates that the proposed approach effectively addresses and mitigates the dataset bias issue encountered by previous methods, thereby significantly enhancing accuracy.

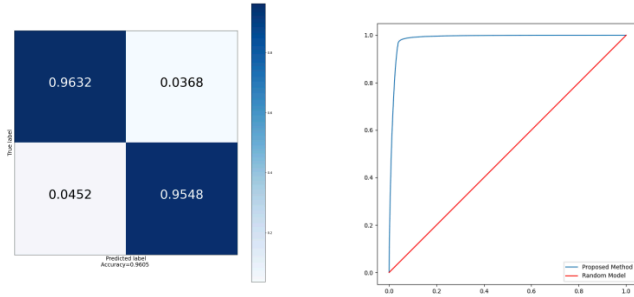


Figure 11. Confusion matrix and ROC curve (Metastatic Tissue dataset)

Figure 11 displays the confusion matrix and the ROC curve for the methods implemented on the Metastatic Tissue dataset. Similar to the observations in Figure 9, the results show the stability and consistency achieved by the proposed approach.

4.2.3 Ablation Study

To assess the effectiveness of the proposed approach, an ablation study was conducted. The experiment involved comparing the performance of two sets of convolutional neural network architectures. The first group comprises ablation models trained without the proposed approach, relying solely on a supervised manner. The second group includes models trained using the proposed approach.

Table 3. Ablation study results (Breast Cancer dataset)

	Accuracy (ablation model)	Accuracy (proposed method)
VGG19	0.7802 (± 0.0008)	0.8068 (± 0.0011)
MobileNetV2	0.7834 (± 0.0009)	0.8087 (± 0.0014)
EfficientNet-B7	0.7895 (± 0.0014)	0.8157 (± 0.0013)
Xception	0.8267 (± 0.0011)	0.8524 (± 0.0011)
HRNet-w32	0.8480 (± 0.0009)	0.8787 (± 0.0012)
Resnet-50	0.8528 (± 0.0013)	0.8842 (± 0.0008)
Densenet-121	0.8810 (± 0.0010)	0.9148 (± 0.0011)
ResNeXt-101	0.8872 (± 0.0007)	0.9224 (± 0.0013)

Table 4. Ablation study results (Metastatic Tissue dataset)

	Accuracy (ablation model)	Accuracy (proposed method)
VGG19	0.9118 (± 0.0011)	0.9359 (± 0.0014)
MobileNetV2	0.9151 (± 0.0014)	0.9374 (± 0.0013)
EfficientNet-B7	0.9146 (± 0.0009)	0.9381 (± 0.0007)
Xception	0.9129 (± 0.0012)	0.9424 (± 0.0006)
HRNet-w32	0.9174 (± 0.0008)	0.9442 (± 0.0006)
Resnet-50	0.9129 (± 0.0013)	0.9481 (± 0.0012)
Densenet-121	0.9253 (± 0.0016)	0.9599 (± 0.0011)
ResNeXt-101	0.9287 (± 0.0007)	0.9605 (± 0.0010)

Table 3 provides a summary of the evaluation results for the Breast Cancer dataset, while Table 4 presents the results for the Metastatic Tissue dataset. Remarkably, the evaluation results of the proposed method consistently outperform the ablation model across all convolutional neural network architectures by a significant margin. This outcome demonstrates that the proposed approach effectively addresses the dataset bias issue inherent in supervised training methods. The superiority of these results can be attributed to the proposed contrastive learning-based representation learning which aims to train the model to extract latent patterns of cancer cells.

5. Conclusion

This research has aimed to revolutionize the landscape of pathology image analysis, specifically targeting Whole Slide Images (WSIs), by introducing a novel contrastive learning-based multi-task system. The experimental results demonstrated the efficacy of the proposed approach in enhancing the accuracy and reliability of whole slide image classification. The proposed system, leveraging contrastive learning techniques, has consistently outperformed existing state-of-the-art machine learning models, as demonstrated in the evaluation on both Breast Cancer and Metastatic Tissue datasets. Notably, the proposed system exhibited stability and consistency across diverse datasets, addressing the bias issues encountered by previous methods and achieving remarkable performance metrics above 90%. This research contributes to the field in several key ways. First, it addresses the time-consuming and labor-intensive nature of traditional pathology processes by automating whole slide image classification. Second, it tackles the bias problem inherent in machine learning models which ensures their adaptability to real-world scenarios. Third, the proposed system provides a robust and consistent approach to pathology image analysis.

The Pulse of Progress: My Summer Journey into Cardiac Surgery and the History and Practice of Coronary Bypass Surgery

Article by **Hermione Wu '27**

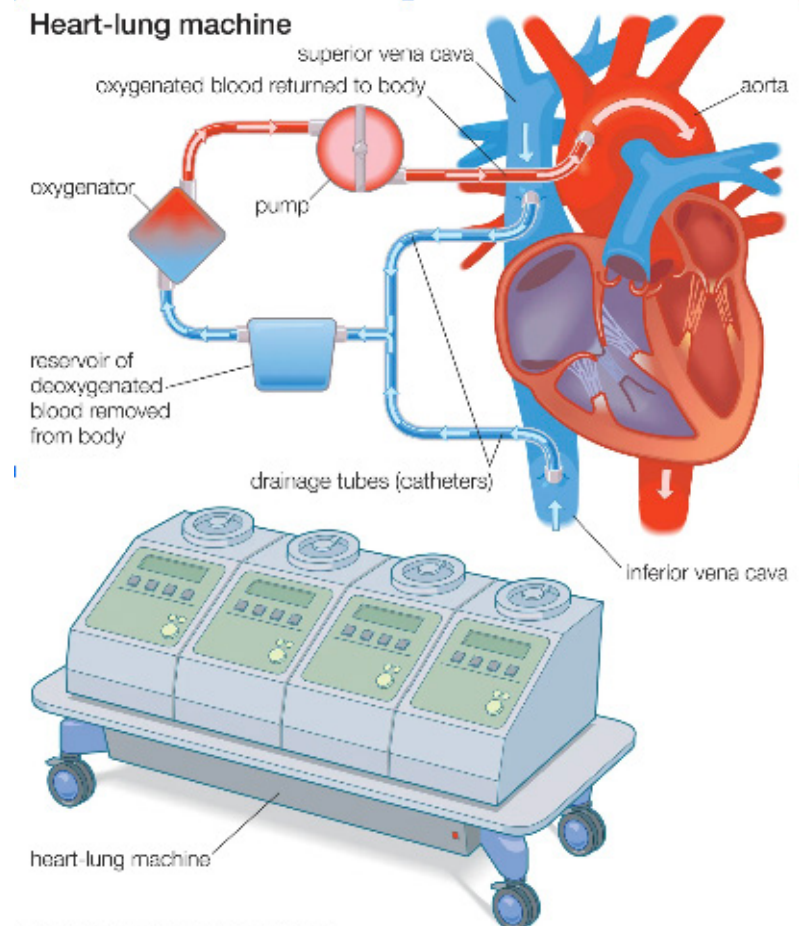
Introduction: American Academy of Medicine & Surgery Surgical Summer Program

Every meditation guide I have used in an attempt to escape from either insomnia or stress tells me to remain still and notice vital sensations going on internally in my body. They will guide my attention to involuntary movements such as my breath and my heartbeat. The heart beats and pumps blood restlessly and is often referred to as the “city pump” of our body. I have often pondered how surgeons would be able to cure someone if their heart isn’t pumping.

This summer, I attended the American Academy of Medicine & Surgery (AAMS) surgical skills internship program to learn about cardiac anatomy and physiology and develop fine motor skills for young aspiring surgeons at UCLA, where I, along with my peers ranging from high school, pre-med, and medical students acclimated to performing basic and advanced cardiothoracic surgical procedures on pig hearts. During the second week of the program, my childhood question untangled like Rapunzel’s hair as I learned about the coronary artery bypass graft, aortic valve replacement, tetralogy of Fallot and other very complex congenital procedures my assistant and I performed on actual pig hearts.

Each morning we prepare our “heart of the day” by dissecting unwanted parts and cleaning up the crucial structures that would be used in the lab that day. Fats, collagen, and other materials would have different textures, creating different sounds and experience when cutting into it. The aorta and other major heart vessels are always the top priority to preserve and I would go through on average 5 minor “heart attacks” each morning, hallucinating upon the fear of destroying the important vessels. “Heart attacks” as I say, but myocardial infarction (MI) is the more technical term. Fortunate enough, one of the first complex procedures we learned at this program is one that repairs a common type of heart attack.

Like our body, the heart muscles (myocardium) require the supply of oxygen and nutrient properties to function properly. One common type of malfunction occurs in the coronary artery, which is located on the posterior side of the left ventricle. Coronary artery disease (CAD) happens when coronary arteries struggle to provide sufficient oxygen and nutrients. Hence, when a narrowing (stenosis) or a blockage occurs in the coronary arteries, the heart subsequently suffers from a lack of oxygen and nutrients, which can cause myocardial infarction (MI) and other lethal coronary artery diseases (CAD). One of the most commonly performed and accessible cardiothoracic surgeries in the world aims to cure certain types of CAD. This surgery is called the coronary artery bypass graft surgery (CABG).



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Figure 1. Simulated Diagram of where catheters are placed to show how the heart is connected to the heart-lung machine.

Brief history of the development of CABG

The history of coronary artery bypass procedures can be traced back 100 years. In 1910, surgeon Alexis Carrel operated with a vascular transplant in dogs to “shrink” an irregularly enlarged aorta, known in medical terms as “intrathoracic aortic”. This opened up development in vascular transplant technologies and inspired the usage of grafts in coronary surgeries to repair or replace vessels in the coronary circulation.

One significant complication that impeded the development of procedures in the coronary arteries is the need to operate on an arrested, non-beating heart. Patients faced great risk due to inadequate blood flow and oxygenation in body organs.

Surgeons used primitive methods such as hypothermia to curtail the metabolic demand of the patient by way of decreasing body temperature below negative 35 to 25 degrees Celsius. In 1953, this changed with the innovation of the heart-lung machine. The heart-lung machine, otherwise referred to in this article as the cardiopulmonary bypass, was fully developed and commonly used in cardiothoracic surgeries in the late 1950s and early 1960s. The first successful open-heart surgery using a heart-lung machine was performed in 1953 by Dr. John Gibbon of the Thomas Jefferson University Hospital in Philadelphia.

The machine allowed heart surgeons to temporarily institute cardiopulmonary bypass to surrogate the function of the heart and lungs during open heart procedures while continuously maintaining blood circulation and oxygenation to the body by exsanguinating the Right heart via superior and inferior vena cava to the oxygenator (collects, oxygenate, filters, warms, or cools the blood), supplying it back to the body via the ascending aorta. This made open-heart surgeries much more feasible, allowing for procedures like CABG to perform safely.

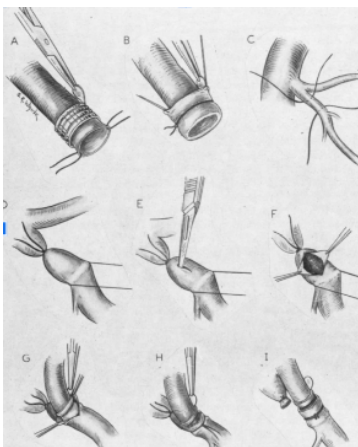


Figure 2. technique of non suture coronary-mammary artery anastomosis.

The 1960s to 1990s marked a phenomenal development in the coronary artery bypass graft operation. Operations prior to the first CABG surgery mainly focused on curing coronary artery disease through expanding and repairing the coronary arteries, but the usage of graft to completely replace a part of the artery has never been performed on human patients. Robert Goetz and his team at the Albert Einstein College of Medicine-Bronx Municipal Hospital Center in New York successfully performed the first ever CABG surgery using tantalum rings and the saphenous vein graft. The procedure involves mobilizing the saphenous vein and connecting it to a coronary artery without sutures but using specially designed tantalum rings which allowed for anastomosis (connections between arteries/vessels), reducing the risk of myocardial ischemia during surgery.

Dr. Robert Goetz’s surgery was pivotal; however, the issue lies within graft patency, particularly, the usage of vein grafts lowers the success rate of the surgery which made them prone to complications such as thrombosis and restenosis.

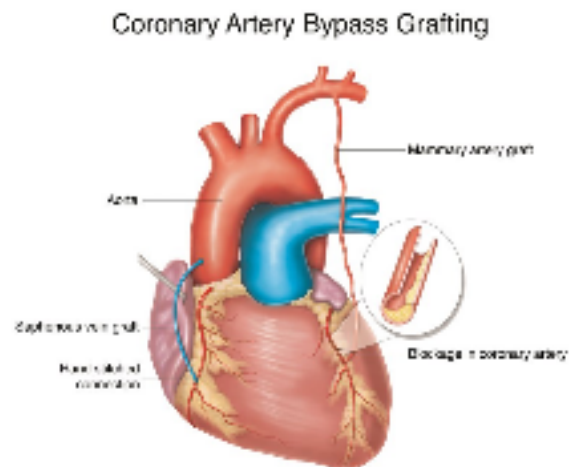


Figure 3. Diagram displaying how and where the mammary artery graft bypasses the blockage in the coronary artery into the ascending branches-off aorta; on the left, how a saphenous vein graft does a similar function.

Nowadays, the operation of using a conduit from the patient’s own body to solve coronary artery disorders can either be performed under various conditions and with multiple choices of the conduit, no longer limited to veins: internal mammary artery, radial artery, or saphenous vein. This operation, once considered as a complicated surgery, is now almost a routine in many medical centers as “Coronary artery bypass operations are now performed half a million times a year with an overall success rate of almost 98 percent” (Columbia surgery team, 2024). The next section of this article will walk you through a detailed procedure of how a CABG is performed nowadays in the operation room.

The Procedure

Like all procedures, there will be a list longer than your CVS receipt of the tests needed to be run to ensure that a patient is prepared for and capable of undergoing this procedure. After the operation room is prepared, general anesthesia is administered and the patient becomes unconscious, pain-free, with stable vitals with the chest open down the sternum and the heart properly assessed. The patient would also be given an injection of heparin to prevent blood coagulation during the procedure and reduce risk of a stroke.

Then comes the harvesting of the graft that should be used as a conduit. The majority of the patients would be advised to choose their internal mammary artery as the graft, however, the other two choices available are radial arteries and the saphenous veins. Let's take the internal mammary artery as the most common case as the demonstration described in this article. The internal mammary artery (left and right are both feasible), an artery that supplies the anterior chest wall and the breasts that runs along the sternum would be separated and extracted the length needed.

Immediately after, the patient would be put on to bypass the aforementioned heart-lung machine. A cannula would be placed in the superior and inferior vena cava to drain the patient's blood before it enters the right atrium and another in the aorta so that the heart-lung machine will ensure a stable but manmade pulmonary circulation. The surgeon would then clamp the ascending aorta below the cannula and give a dose of potassium solution to the coronary artery to temporarily stop the heart. It is extremely important to notice the location of where the aorta should be clamped as if the potassium solution enters the bloodstream that supplies the body, it could lead to fatal effects on the patient. Now that we have the heart drained of blood and not pumping, we can proceed to attaching the graft onto the coronary artery.

After the patient is put on bypass and the graft is harvested, a small incision would be made on the coronary artery that has a coagulation. One of the most fundamental and important surgical techniques I learned at my summer program was how to correctly suture the graft onto the coronary artery.

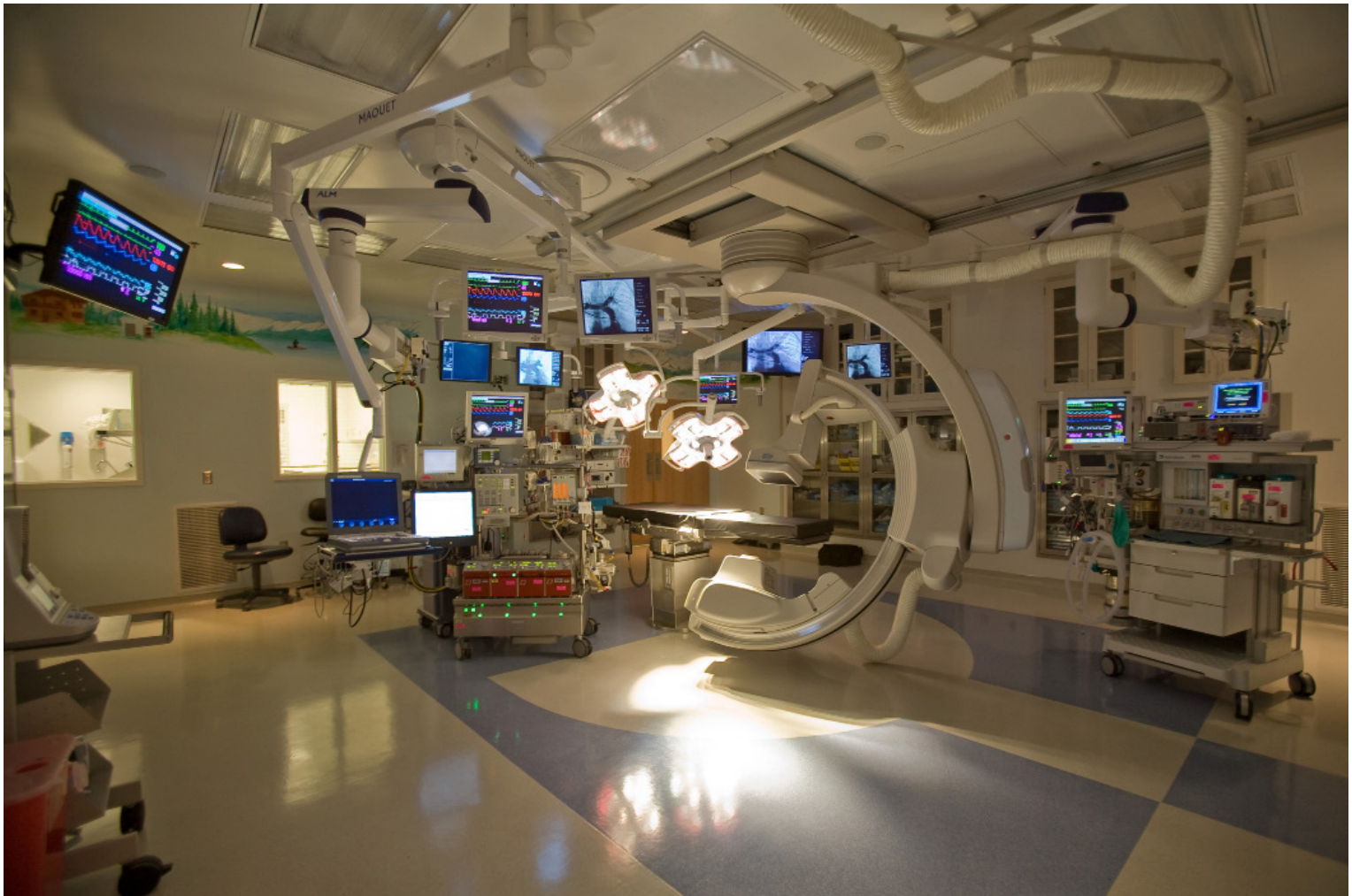


Figure 4. Cardiac Surgery Operating Room



The surgeon should envision both the incision on the artery and the side of the graft as a clock. Sutures should run in the “opposite” number on the “clock”: sutures running in on 5 o’clock on the incision should come out on 7 o’clock of the graft, 4 o’clock should go to 8 o’clock, and so on.

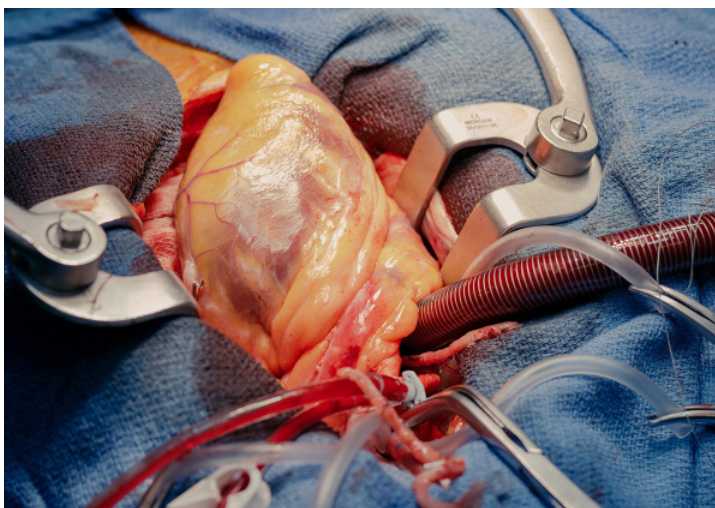
Sutures should always run in the pattern of “out-in, in-out,” meaning that the needle should run from the exterior to the interior of one surface, and go from the internal face out of the other surface. With this, one side of the graft should be attached onto the coronary artery and the other side attached to the aorta. Before closing off the chest the surgeons can run saline through the graft to confirm that the graft is functioning properly.

This bypass creates a new pathway for oxygenated blood supply to flow to the heart muscles and serves as a vital option in the management of coronary artery diseases. The innovation of this procedure significantly decreased the lethal rate of coronary artery diseases. Currently as one of the most commonly performed open-heart surgery, it laid the foundation of the development of more advanced cardiothoracic surgeries and more innovations in the medical field.

As amazing the medical field has been with curing diseases and helping us thrive, our body is the true wonder. So, next time during a guided meditation, feel your heartbeat, love your heartbeat, and remember how your existence is already a gift to this world.

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Optimal Guessing Strategy

1 Introduction

This paper was inspired by a task in Dr. Fisher's HS150 (Introduction to Philosophy) class. We were given a Question Bank, a non-graded, multiple choice test featuring all of the possible questions for the upcoming graded assessment, each having four options. Students can take this test an unlimited number of times, seeing their score after each attempt but not which problems they answered correctly. I began to wonder how I could find the right answers in the least amount of attempts possible. To start, I made three different strategies: the non-intelligent, the semi-intelligent, and the intelligent strategies. The non-intelligent strategy consists of arbitrary repeated guessing on all of the questions with no other methods involved. Simply put, it is a random guess. The semi-intelligent strategy involves a more developed method of guessing, but with the knowledge of the inputted answers for each question and their scores from previous attempts. For example, if the score was a 3/10 on the first attempt, it will remember both this score and all the answers inputted to make the best strategy for the second attempt. However, it lacks the key feature that sets it apart from the intelligent strategy—the ability to deduce the answers to certain questions based on changes in scores when different answer choices are selected.

For example, if the first attempt resulted in a score of 1/10 and the student changed a wrong answer to a right one, which resulted in a new score of 2/10, the intelligent strategy would deduce that the answer that the student changed is correct. By contrast, the semi-intelligent strategy can not do this. This paper discusses the optimal semi-intelligent strategy in how it finds all the right answers in the least amount of attempts for the Question Bank test.

2 Optimal Semi-Intelligent Guessing Strategy

2.2.1 Overview of Strategy

By definition, our semi-intelligent guessing strategy strictly remembers the inputted answers and scores from the previous attempts. Thus, the semi-intelligent guessing strategy consists of guessing on a specific number of randomly selected questions. It can only guess because although it does remember what the student has put on the questions previously, it can never deduce if the answers were correct.

Article by Dawson Park '28

This may seem counterintuitive because students can easily deduce that by changing one answer to one question from our previous attempt and we find that our score increased by one, then the answer that we changed must be correct. For example, if there are 10 total questions and our previous score was a 3/10, then the semi-intelligent strategy would calculate the number of answers to change from the previous attempt to produce the highest probability of increasing the score. This can be generalized to the situation where there are k total questions on the test and the previous attempt gave n questions correctly, the semi-intelligent strategy will find the optimal number of questions to change such that the score improves the most.

2.2 Calculations and Finding the Strategy

To find this strategy, I first defined a function with parameters k and n , where k is the total number of questions and n is the number of questions answered correctly in the previous attempt. I then made a loop that looped through all the possible number of answers it could change, y . This ranged from one answer changed to all answers changed. My main goal was to find the probability of increasing the score the most for each given number of answers changed. Then, I made a second loop which looped through all the possible numbers which the score could increase by, given the number of answers changed. When only taking into account positive increases, the range of increase in score is $[1, y]$, where y is the number of answers changed, because the score can only change as much as the amount of answers changed.

2.2.1 Motivation

My goal was to find the probabilities of each possible increase in what I did above. What this means in simpler terms is that I was first trying to find the probability of increasing a specific number, x . Let us denote this probability by $P(x)$. Then, we can multiply $P(x)$ by x and summing these products, $P(x) \cdot x$, letting x range from 1 through y . This will give the total expected increase when we change y answers.

2.3 Calculations and Generalizations

We will begin with a summary of what we have in the function so far. We first made a loop, looping through all the y , the possible number of answers we can change. Then, within that loop, we loop through all the possible m , the number of points our score can increase by. Now, we just have to find the probability of increasing our score by m , by changing y answers from the last attempt, given that we started with n correct and k total questions on the test. Again, we will make another loop, looping through i , the different possible number of previously correctly answered questions we change. Simply put, if we are changing 4 questions with 5 questions answered correctly, then the different possible number of previously correctly answered questions we can change is 1, 2, 3, and 4. Now, we have narrowed this down to a very specific sub-problem. Our goal is to find the probability of increasing our score by m questions by changing y answers from the last attempt, where i of those y changes will be changing previously correctly answered questions. First, when we change the answer of a previously correct answer, we change i answers to questions that were previously correct, thus decreasing our score by i . This means that in the other $y-i$ changes we make to previously incorrect questions, $m+i$ must be correct. In the end, we get a net increase of

$$m + i - i = m$$

To find the probability, we first need to find the number of ways to choose the modified correct answers as well as the incorrect answers we change. As defined earlier, there are n previously correct questions, which means that there are $k-n$ previously incorrect questions. We are choosing i of these n correct answers to modify, and $y-i$ of the $k-n$ incorrect answers to modify because in changing a total of y questions with i questions being correct, then $y-i$ are going to be incorrect. So, the two different combinations we multiply are:

$$\binom{n}{i} * \binom{k-n}{y-i}$$

However, we must divide this above product by the total number of ways to choose y questions from k total questions because we are trying to find probability. Thus, we get:

$$\frac{\binom{n}{i} * \binom{k-n}{y-i}}{\binom{k}{y}}$$

Still, we are far from done. Back to three paragraphs above, we see that in the number of $y-i$ changes we make to our incorrect answers, $m+i$ of them must be correct. This is a good time to touch upon what happens when we change a previously incorrect question: we either change it to the correct answer, or to another incorrect answer. The probability of changing it to the correct answer is $1/3$ because there are 3 different answer choices to change it to, and only 1 of them are correct. So, the probability of changing the answer to another incorrect answer is $2/3$. Going back, since $m+i$ changes of the $y-i$ total changes to previously incorrect answers must be changed to a correct answer, we have to multiply by a combination of:

$$\binom{y-i}{m+i}$$

We are very close to being done, but we still need to multiply by probabilities of changing previously incorrect answers right or wrong answers. Since we need to change $m+i$ of previously incorrect answers to correct answers we have to multiply $1/3$ by itself $m+i$ times. Next, since we have to change a total of $y-i-(m+i)$ of those changes are going to be changed to another incorrect answer. This means that we need to multiply $2/3$ by $y-m-2i$. Finally, putting all our products together, the probability is:

$$\frac{\binom{n}{i} * \binom{k-n}{y-i}}{\binom{k}{y}} * \binom{y-i}{m+i} * \frac{1}{3}^{m+i} * \frac{2}{3}^{y-m-2i}$$

This multivariable function calculates the probability of increasing the score by m when changing y total questions, where i of them are changing previously correct questions, and n is the number of questions that were previously answered correctly in a test with a total of k questions. Lastly, we multiply this probability by m to find the expected increase in score. We can run this function through all these loops and sum the expected values for each y to get the expected increase when we change y answers, as y ranges from 1 through k .

Then, by evaluating which y yields the highest sum of expected values, we can determine the best number of answers to change for maximizing the score increase. This is the essence of the problem we were trying to solve. After translating all this mathematical logic into code, we succeed in creating a program that provides the optimal number of answers to change.

3 Conclusion

After all the calculations and coding, I have programmed the optimal semi-intelligent guessing strategy. However, I did take one big lesson out of this problem. After running this program and taking a look at the expected values, I realized that they are surprisingly low. In conclusion, this paper suggests you make an “educated guess” on the next Question Bank test, rather than randomly guessing.

Schizencephaly

Article by Xavier An '28

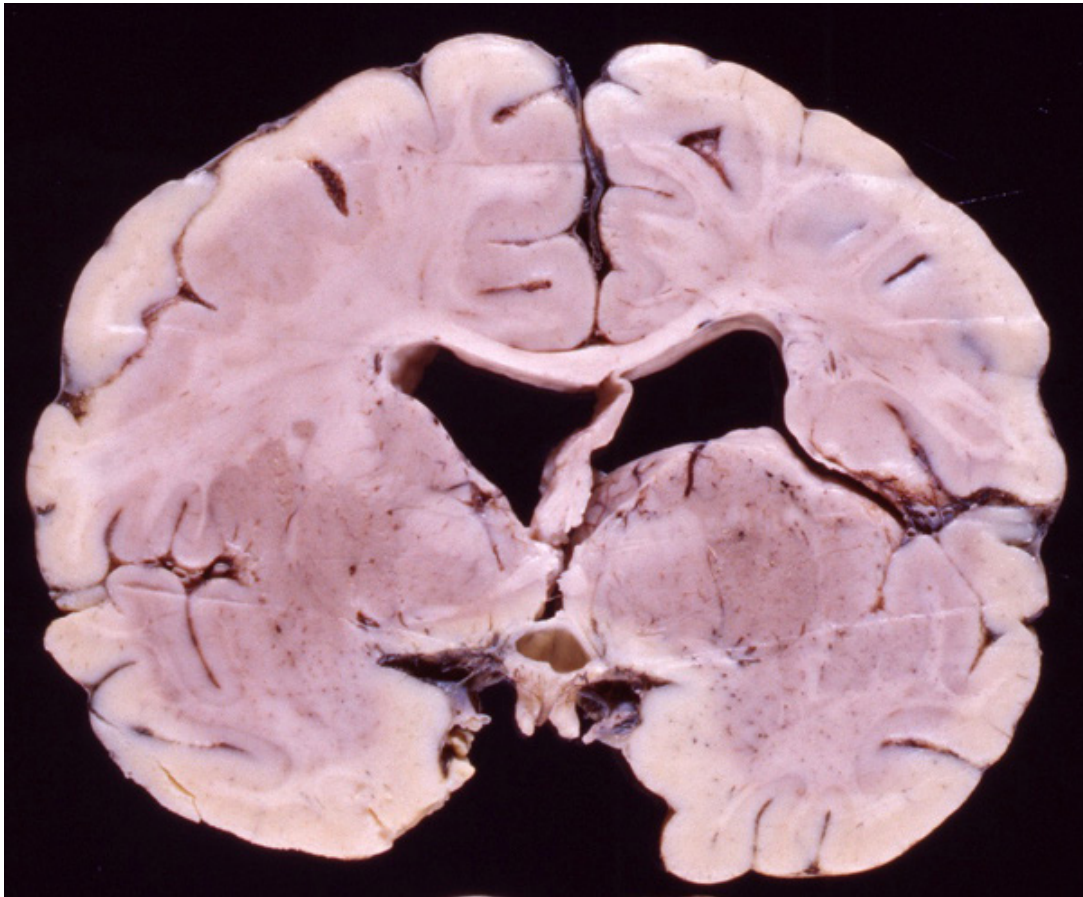


Figure 1: Human Brain Abscess

Abstract

Schizencephaly is a scarce congenital neurological disorder caused by malformations in either hemisphere of the brain. It is identifiable through the many aplastic hollow clefts and cracks visible in the place where the brain was supposed to form. After meticulous research through the limited reference sources of information on schizencephaly and personal experiences, this article reports the types, symptoms, causes, and possible treatments of this truly devastating birth defect. Schizencephaly can be classified into two types: Closed-lip (Type I), where the clefts are closed off inside the brain, and Open-lip (Type II), where the clefts link the interior ventricles of the brain to the outside and lead to more severe symptoms. Some symptoms that a victim of schizencephaly may experience include, but are not limited to: constant seizures, spasticity, paralysis, hydrocephalus, and development delays in communication, gross/fine motor, and cognitive skills.

The causes of schizencephaly in most cases are sporadic genetic variations or environmental factors during pregnancy, such as medical substances or viruses. Diagnoses of schizencephaly are made by CTs or MRIs. Treatments vary based on the symptoms and severity of the case, but most entail seizure treatment from drugs or therapy, developmental therapies to assist and improve motor and cognitive deficits, and regular neurological evaluation.

Approximately 1.49 babies are affected by schizencephaly per 100,000 born; the seemingly low incidence does not render it any less of an important topic to be aware of, as tentative treatment or hasty generalization may cause great tragedies.

Navigating the Complexities of Schizencephaly: Insights into Rare Brain Disorders

Introduction

The human brain is the most complex organ within the human body. It controls everything that defines our humanity: our thoughts, memories, emotions, and actions. The term “schizencephaly” is derived from the Greek words “schizein” (to divide) and “enképhalos” (the brain). In the world today, neurology disorders play a threatening and expanding role, causing pain and grief to families around the world.

My twin brother was born with an extremely severe case of schizencephaly. During the early stages of my mother’s pregnancy, it was hard to distinguish any problems through X-rays, especially since the fetus was a twin. However, as my mother’s gestation continued, the longitudinal fissure in my brother’s brain grew abnormally wide. After we were born, his case wasn’t quite identifiable at an early age, as he behaved indistinguishable from any other baby; but while I slowly learned to talk and walk as we both matured, he would not develop these skills. He had to be constantly fed, cared for, and put to sleep, while suffering through seizures and a range of other troubling sicknesses.

Initially, I naively thought that he was just less intellectually developed, and would sometimes even feel slightly appalled by him. But as I slowly became inquisitive about his case and understood more, my parents told me the truth. Moments before we were delivered, devastating news hit my parents. After a precise computed tomography scan, my brother was diagnosed with open-lip (Type II) schizencephaly.

To this day, he has still not learned how to communicate, walk, or do anything by himself, and is only able to laugh or cry. I often go down to his room to read him stories in English and Chinese or push his wheelchair around on the paths outside of our house, to bring him warmth and get closer to him. A small dream of mine is to find a cure for this disease since it does not currently exist. That is why I am writing this paper today.

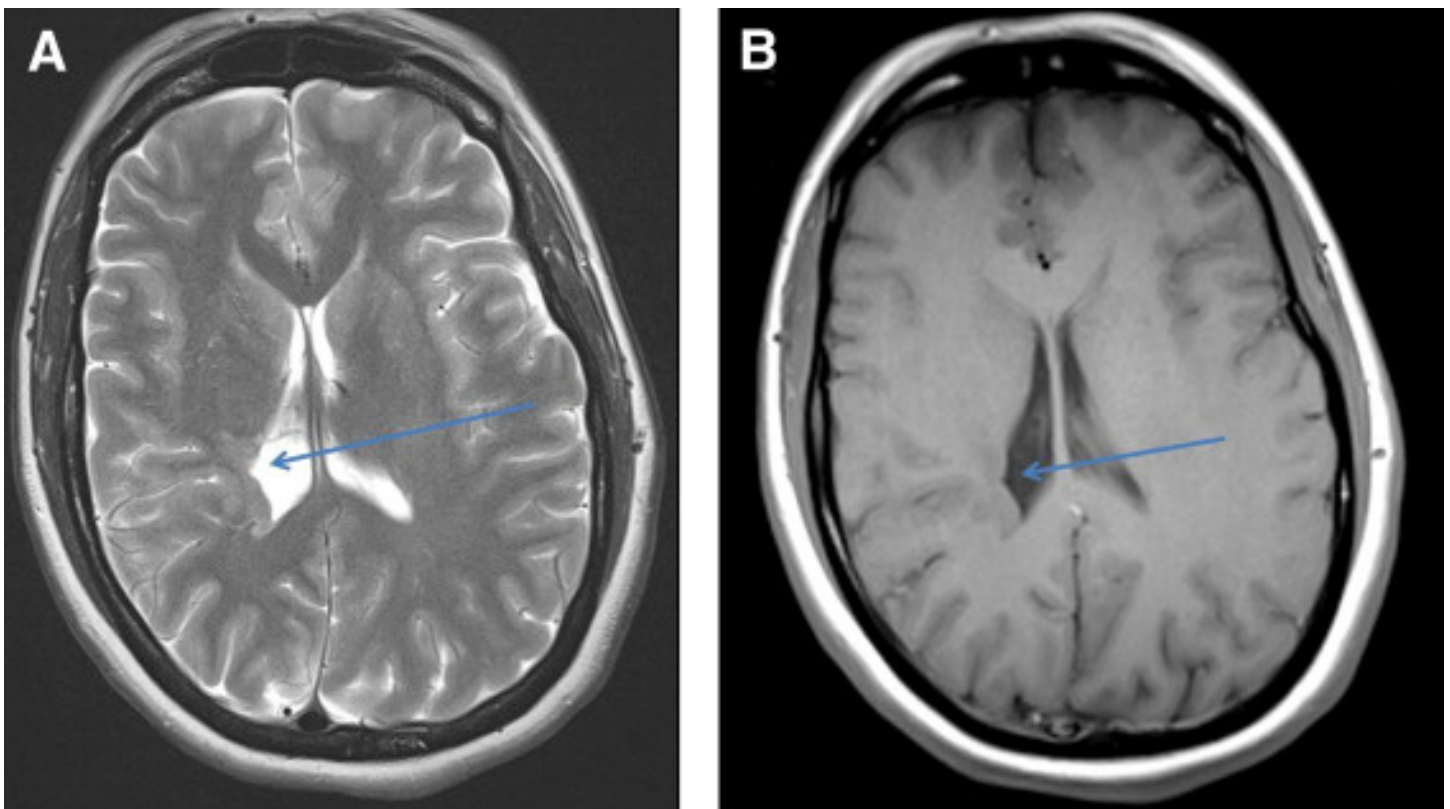


Figure 2: Type I Schizencephaly (closed lip). Axial T2 (A) and T1 (B) weighted images show a subtle beaking of the ventricle (arrow). There is heterotopic grey matter lining the ventricle and extending from the ventricle to the surface of the brain.

Types and Symptoms

Schizencephaly is a type of cortical malformation, where cells that must migrate from parts of the brain to another do not do so entirely. It is such a rare and unique disorder that it is impossible to be captured in one specific symptom of the afflicted. In the human brain, clefts that form in the cerebral hemispheres contain cerebrospinal fluid (CSF) and gray matter. When the brain is correctly formed, CSF protects and transfers nutrients through the brain, and gray matter regulates memories, movement, and emotions. However, due to schizencephaly, these substances may be absent or excessive depending on the two types, closed-lip (Type I) and open-lip (Type II), severely impacting the brain's performance

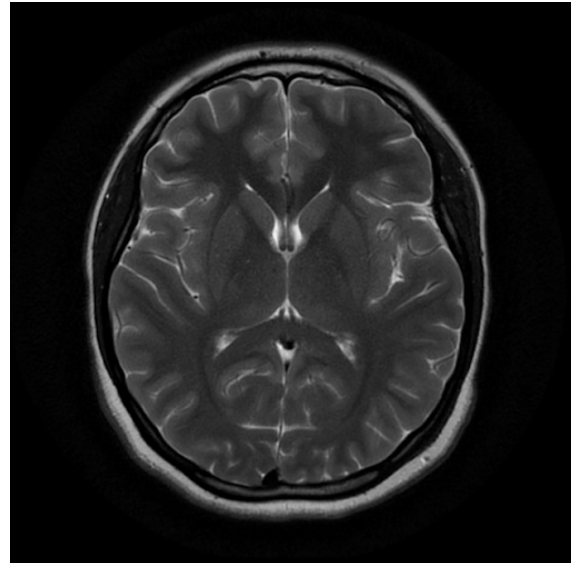
Closed-lip schizencephaly is identifiable through the shorter clefts that form in the center of the cerebral cortex and do not adjoin with the outside of the brain. This allows gray matter to form along the sides of the clefts, and although usually underdeveloped, still helps in limiting the disruption of schizencephaly to the brain. CSFs do not fill the clefts in closed-lip schizencephaly, since the clefts do not reach the two lateral ventricles where CSF is produced. This renders it less dangerous than open-lip (Type II) schizencephaly.

In open-lip schizencephaly, on the other hand, the cleft extends from the outside of the brain. Since there is no tissue fused with the cleft, it permits the flow of cerebrospinal fluid into the subarachnoid space. Consequently, gray matter is absent within the cleft, leading to significant functional disruptions to normal neural connections.

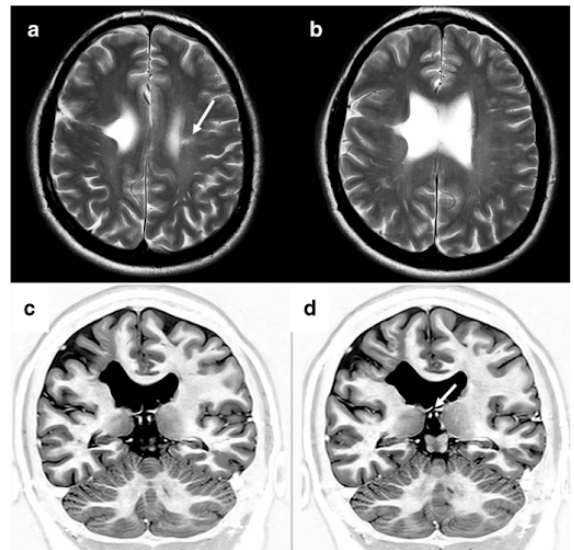
The two types of schizencephaly have similar symptoms, but individuals experiencing open-lip (Type II) tend to have more severe complications. Both types include, but are not limited to, the following symptoms:

1. Motor and cognitive delays (severe motor impairments in open-lip schizencephaly)
2. Seizures, developmental delays, and motor deficits
3. Hydrocephalus (less frequent in closed-lip schizencephaly)
4. Sensory impairments, speech difficulties, and additional structural abnormalities in the brain
5. Spasticity and paralysis
6. Intellectual disorder

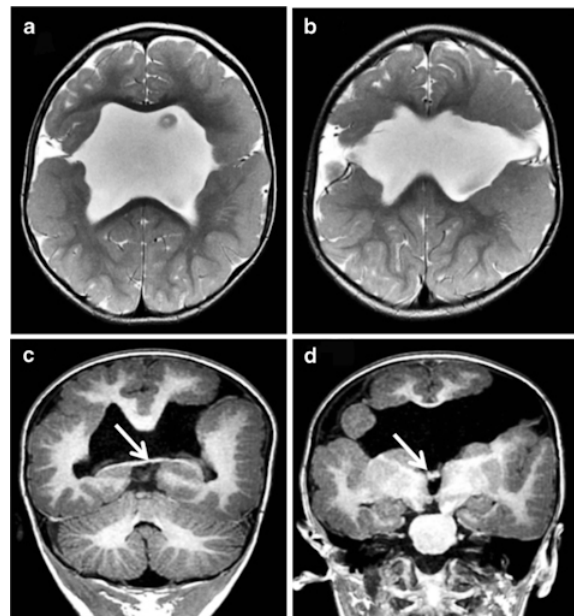
MRI Image of a human brain



Closed-lip Schizencephaly (Type I):



Open-lip Schizencephaly (Type II)



Causes, Diagnosis, and Treatment

To this day, the exact etiopathogenesis for schizencephaly has not been clearly identified by neurologists. Schizencephaly is a congenital neurological disorder, since it happens during gestational brain development. Accordingly, researchers have determined several possible factors: the disorder may be associated with a genetic mutation that affects brain development, inherited from parents, or caused by a sporadic occurrence during fetal development. Genes that are responsible for schizencephaly may be: *EMX2* (responsible for cortical migration), *SIX3* (responsible for development of forebrain), *SHH* (responsible for creating SHH protein) or *OL4A1* (responsible for creating type IV collagen).

Environmental factors, such as maternal infections, prenatal exposure to toxins, and other health conditions, may also play a role in the cause of this neurological disorder.

To detect schizencephaly, the methods of choice are magnetic resonance imaging (MRI) and computed tomography (CT). MRI uses strong magnetic fields and radio waves to detect clefts and detailed images of their characteristics, while CT uses X-rays to detect the presence of clefts. A CT may not provide the same level of detail as an MRI (such as on the images of gray matter) but it is much faster and affordable. The defects from schizencephaly only become apparent during the second half of pregnancy, as the brain develops and forms.

There is no direct method to cure victims of schizencephaly in the present day, and the main treatments for schizencephaly focus more on alleviating and managing the symptoms. Options include, but are not limited to:

1. Drugs or therapy to prevent seizures
2. Physical therapy to relieve spasticity
3. Rehabilitation for motor deficits and intellectual disability
4. Early diagnoses and precautions taken during pregnancy are also critical to optimizing outcomes and providing support.

Conclusion

Ultimately, the severity of schizencephaly depends on variables of the cleft. Schizencephaly was first described by Wilmarth in 1887, but even to this present date, there hasn't been a direct way to cure schizencephaly and let the victim have an opportunity to escape its symptoms. It affects the development of the brain abnormally, with significant impairments of motor, cognitive, and sensory aspects. Although the exact cause remains unclear, genetic and environmental factors contribute to its development. In the future, raising awareness and supporting research is crucial for finding more effective treatments and a cure as we learn more about schizencephaly.



Figure 3: MRI Machine

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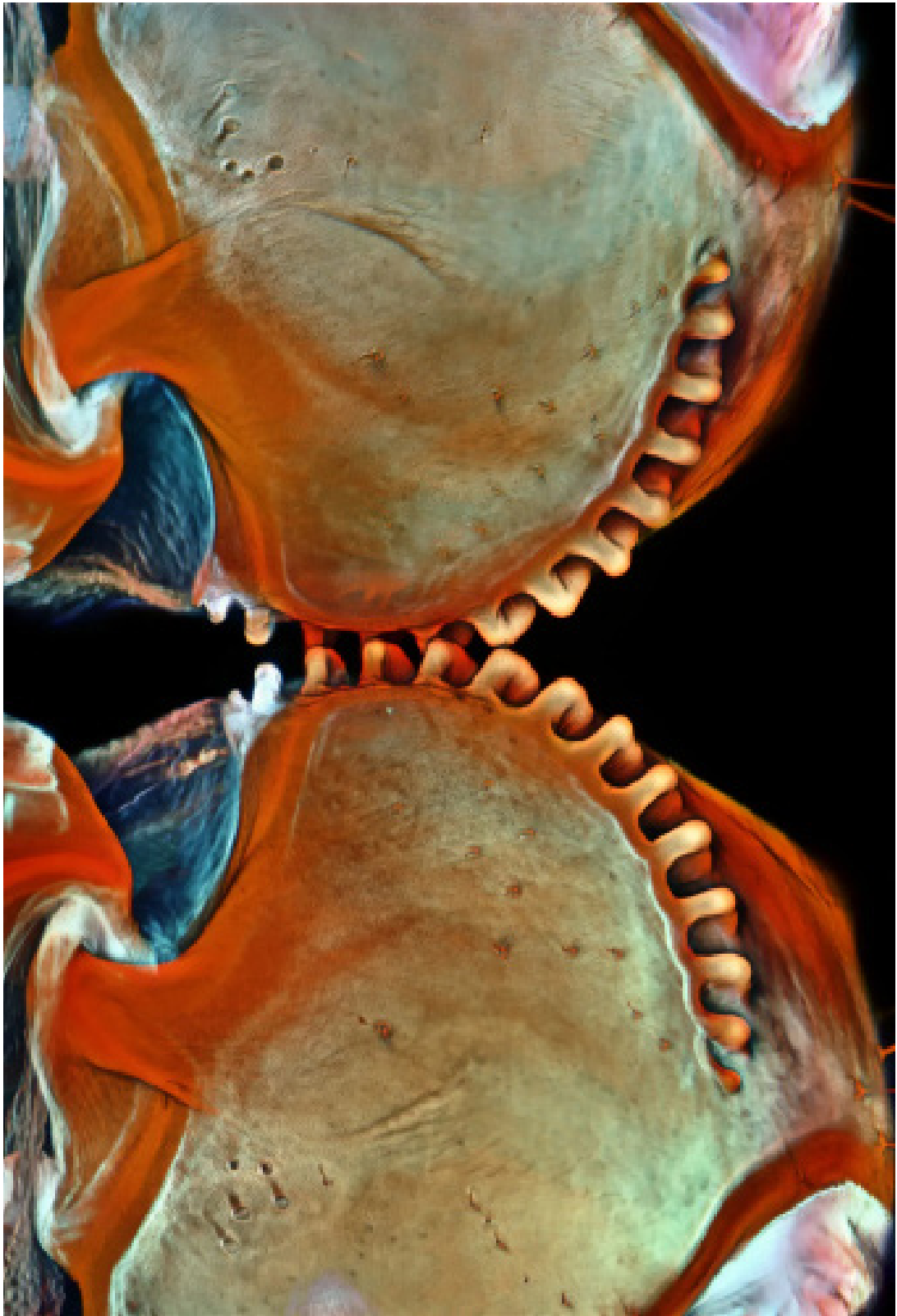
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