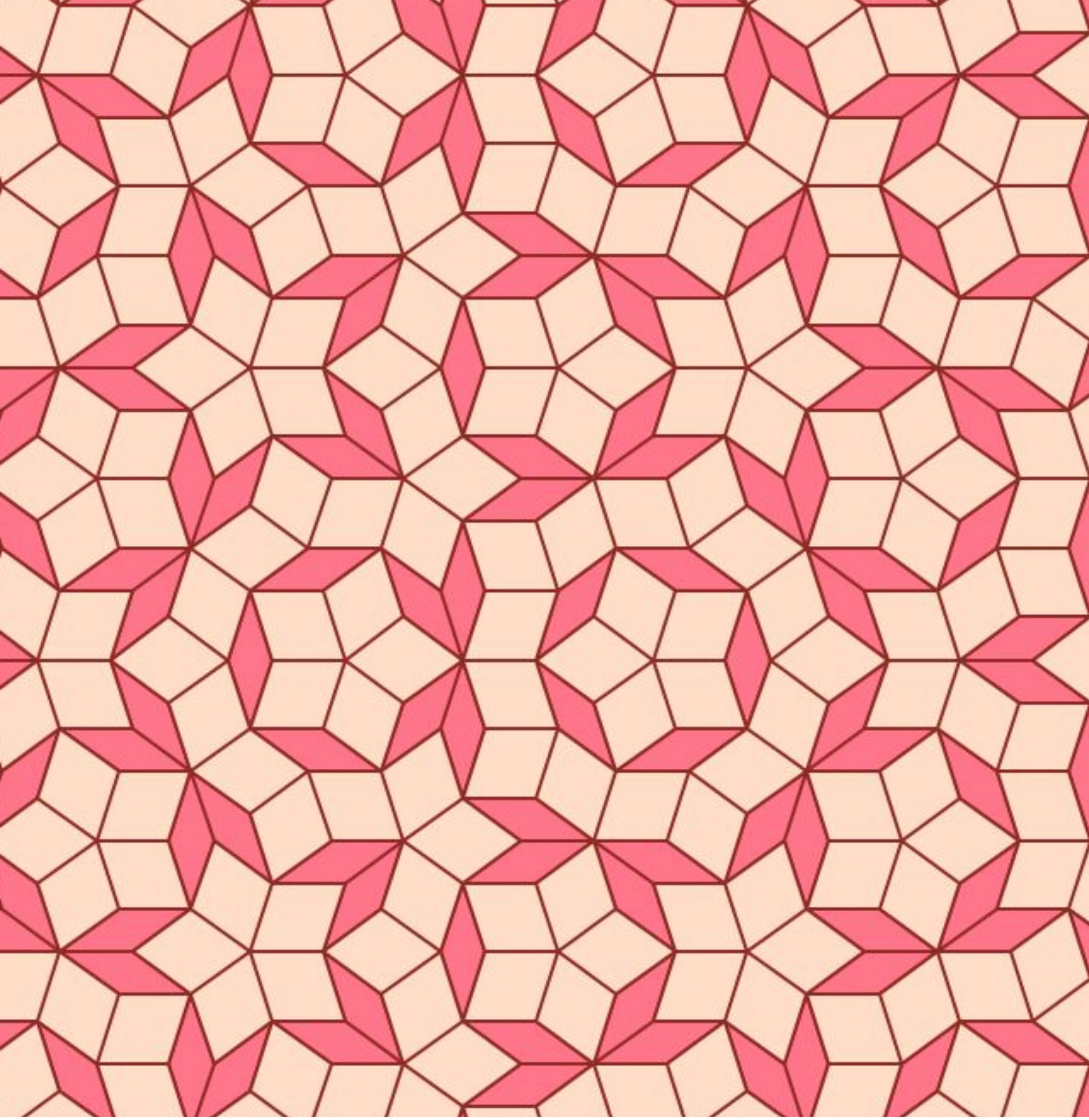

THE PENROSE MAGAZINE

STEM

Issue 8, 2 June 2026

Welcome to the Eighth Issue of Penrose Magazine!

Penrose is a STEM magazine where we hope to establish a community of young people who are passionate about STEM and want to share with their peers and further their knowledge beyond the curriculum. This installment of the magazine consists of the academic articles from the mechanisms behind satellites to photosynthesizing slugs. We hope to continue fostering an environment where people are encouraged to push themselves to create meaningful work and support each other to grow.

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The Mechanisms Behind Satellites

Introduction

Satellites are heavily engineered systems sent to orbit around the Earth to gather valuable data for humans back on the surface. These systems rely on meticulously developed technology to ensure that it does not prove a risk to Earth or to other satellites. Since the launch of Sputnik 1 by the Russians, satellite technology has expanded and developed rapidly. This does not mean that satellites do not still come with their own issues, such as the presence of space debris, pollution. Nevertheless, satellites are the backbone of space travel and data collection, and current innovation promises much more development up ahead.

Mechanisms

Satellites are artificial objects launched into space to perform scientific, commercial, navigational, and military functions. They are delivered beyond Earth's atmosphere by rockets which provide them with the necessary velocity to overcome Earth's gravitational pull and atmospheric resistance [1]. Once a satellite reaches the required altitude and velocity, it enters orbit by achieving a balance between gravitational attraction and forward inertial motion [2].

After orbital insertion, satellites do not require continuous propulsion to remain in motion. The near-vacuum conditions of space reduce atmospheric drag, which allows satellites to maintain velocity with minimal resistance. However, small onboard propulsion systems, typically chemical or electric thrusters, are employed for station-keeping manoeuvres. These adjustments compensate for minor disruptions caused by gravitational influences from the Moon and Sun, solar radiation pressure, and residual atmospheric drag in lower orbits. Thrusters also allow for collision avoidance and end-of-life repositioning.

Satellites orbit in several distinct orbital regimes, the most common being Geostationary Earth Orbit (GEO) and Low Earth Orbit (LEO). Geostationary orbit occurs at an altitude of approximately 35,786 kilometres above the Earth's equator. At this altitude, a satellite's orbital period matches Earth's rotational period, which enables it to remain fixed to a single longitude. This characteristic makes GEO suitable for telecommunications, weather monitoring and broadcasting.

In contrast, Low Earth Orbit ranges from approximately 160 to 2,000 kilometres above the Earth's surface. Satellites in LEO travel at higher orbital velocities and complete an orbit in roughly 90 to 120 minutes. Due to their proximity to Earth, LEO satellites are widely used for Earth observation, remote sensing, and large-scale internet constellations.

Electrical power generation in satellites is primarily achieved through solar arrays which convert solar radiation into electrical energy [3]. Onboard rechargeable batteries store energy for use during periods when the satellite passes through Earth's shadow [4]. Energy management systems regulate power distribution to onboard computers, thermal control systems, and scientific payloads.

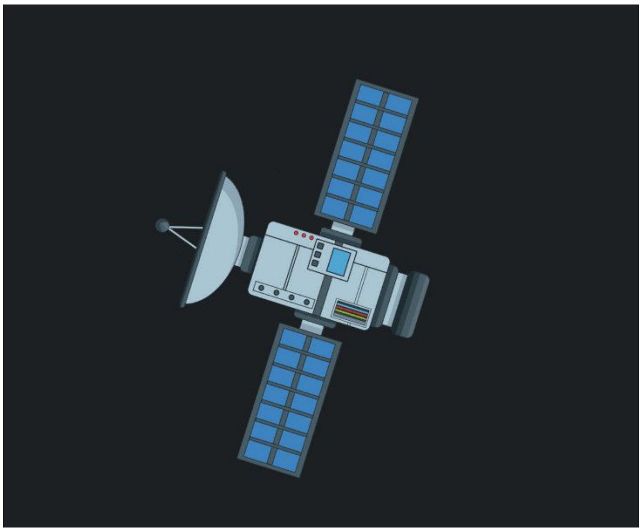


Figure 1: The components of a satellite.

The components of a satellite consist of three principal components: the bus, the payload, and the control systems [5]. The bus constitutes the main structural framework and houses essential subsystems. Satellites can operate for years until their fuel is depleted, at that point they may be moved into a "graveyard orbit" [6].

Uses

Satellites were first used in 1962 as a way to relay telephone, television and other communication [7]. The original satellite was called Telstar 1 and weighed only 78 kg which would be considered very small given newer technological advancement in satellites.

Beyond communication, satellites can also be used for the weather. They carry multiple pieces of specialised equipment, such as radiometers for images and interferometers which are used for measuring the temperature and humidity [8]. Images taken with radiometers are taken in black and white which allows the radiometer to measure visible light. Infrared can be used as a way to measure the temperature on top of clouds, where fewer clouds will result in a higher temperature. The third type that forecasters use is water vapour which shows the moisture content to help reveal information about humidity or level of moisture. Areas which are darker typically tend to be more dryer, though some misconceptions can be created at night [9].

Satellites capture time-lapses by taking multiple snapshots in a short period of time, this gives clues to what happens next, and meteorologists will use models and predictions to be able to forecast the weather.

Television signals are directly transmitted from satellites within a geostationary orbit [10]. These satellites typically lie around 36,000 km above earth and have a time period of 24 hours. These orbits are assigned by the International Telecommunication Union (ITU). Satellites distribute the signal to land-based transmitters, the signal is then received by the transmitter and then broadcast to receivers to consumers (TV's). Whereas cable networks deliver content via terrestrial cable facilities [10].

Since 1983 satellite news trucks have been gathering news and broadcasting live. This is achieved by using trucks with an antenna and a dish which points towards a communication satellite. Audio and video can then be sent to the television company where it is then broadcasted [11].

The United States global positioning system GPS was the first operational satellite navigation system, which was developed in the 70s [12]. A full 24 satellites were fully operational by 1993. The Global Navigation Satellite System can be used to attain an absolute position, which is essential for GPS tracking. The GNSS achieves this by using a receiver called trilateration to calculate an object's location on Earth based on the distance between multiple receivers. GNSS satellites are placed at a medium speed of 20,000km so they can circle the earth every 12 hours. A full constellation of 24 satellites was reached in 1994 and they travel about 7,000 miles per hour [12].

GPS is built into many types of devices such as smart watches, satellite communicators, boats and vehicles and so on. GPS have become extremely accurate due to their multichannel parallel design; however, some other error sources can cause some effect within the GPS, accuracy of GPS is best when on the water as there is no interference [12].

Limitations

Current satellite technologies face several limitations. The most prominent of these is interference. Interference is when the signal between the satellite and the receiver is affected, which may lead to data loss and service outages. This can occur due to several factors: the environment, operating frequency, and receiver technology [13].

Natural attributes of an area, including solar radiation and ionospheric interference, interfere with satellite signals. Extreme cases of solar radiation can result in solar outages. This can be mediated by increasing the aperture or the frequency of the receiver antenna as it can decrease the amount of time a signal is affected by radiation; however, it also results in a decrease in beamwidth. Ionospheric scintillation, caused by the charged layer in the atmosphere known as the Ionosphere, can affect the amplitude and angle of arrival of a signal [14]. This can depend on location, the information length being transmitted, and signal frequency.

Another common cause of interference in satellites is from equipment failure. Issues with the receiver's intermediate frequency (IF) cable can result in weaker frequency bands, making it more difficult for signals to be isolated [14]. Transponders may also generate intermodulation interference due to the equipment's ability to convert frequencies or amplify power.

Estimation errors can lead to additional limitations presented by current satellite technology. Many of these errors stem from the precision of the calculated distance between the satellite and receiver, also known as the pseudorange [15].

$$Range_{measured} = Range_{True} + Satellite\ Clock\ Error \times Speed\ of\ Light$$

The atomic clocks contained on each satellite are extremely precise, though are often asynchronous with each other and their receiver. Recording true time is impractical, so pseudorange is often used instead [15].

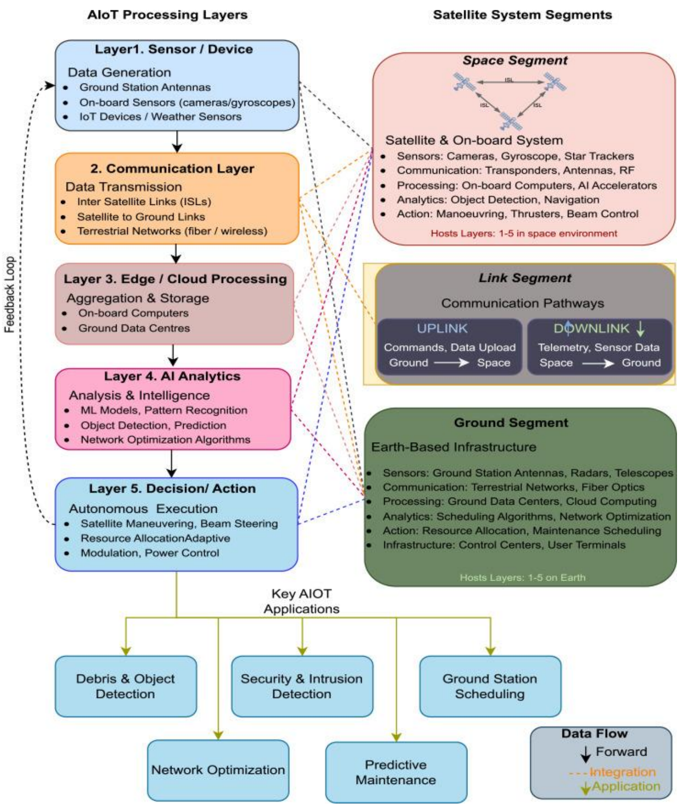
$$Time\ of\ Transmission = Signal\ Reception\ Time\ at\ Receiver - \frac{Pseudorange}{Speed\ of\ Light}$$

Additionally, satellite errors may be caused by multipath. This occurs when a satellite signal reaches its receiver along two separate paths due to signal reflections off other infrastructure [16]. Similarly to estimation errors and uncertainty, multipath can lead to incorrect calculation of satellite position. Multipath errors are more common in areas with crowded infrastructure or reflective material, and can be avoided in more rural locations.

Beyond process limitations, satellites can also encounter issues because of the data they collect. As different periods of orbit may result in different speeds of travel, satellites may be unable to transmit data effectively at certain locations [16]. Furthermore, the limited storage space supplied to a satellite means transmissions should be made often so more data can be collected. Therefore, it is important that satellite signals have sufficient bandwidth to send data effectively.

The Future of Satellites

Emerging satellite technologies are currently moving beyond traditional larger satellites to more adaptable systems based on new computational insight, AI integration, and advanced manufacturing techniques, optimized to reduce cost and improve the range of services satellites provide. A major improvement in next-generation satellite systems lies within the integration of Artificial Intelligence of Things (AIoT) ecosystem [17].



Satellite orbits are often classified into three primary orbits, with LEO being deployed at altitudes ranging from 160 km to 2000 km. Due to its low cost and high connectivity, it is the area attracting most researchers, with over 6,972 satellites now positioned there. Some issues that arise with many systems operating in this space are constant network reconfiguration, advanced resource management, and collision avoidance, which traditional systems cannot efficiently and simultaneously handle.

Where AIoT can help is via a layered system, where satellites, sensors, and ground stations are classified into Layer 1 which is data analysis. Layer 2 involves communication between satellite networks, trans-terrestrial data transfer, and ground to space downlinks. Layer 3 focuses on cloud processing via onboard computers and ground data centers. Layer 4 incorporates AI analytics through ML-based algorithms, and the final layer executes control and actions, such as beam steering.

This allows for adaptive optimization and prediction, reducing reliance on ground control. The integration of AI can also help push other crucial developments in orbital technology like quantum communication by identifying patterns in transmission errors, support network optimization and resource management, as well as designing and simulating quantum communication protocols [18].

Currently, the world's first microsatellite Jinan-1 launched in July 2022 [19]. Jinan-1 utilizes AI to stabilize laser communications during operations. With it, a new possibility in satellite technology emerged in the form of Quantum Key Distribution (QKD). In the pursuit of future secure communication, scientists have explored QKD—a method in which data is encrypted using the fundamental laws of physics [19]. Although proven challenging over long distances for various reasons, the launch of Jinan-1 became a significant step in solving that issue by demonstrating feasibility in real-time long distance communication.

The satellite uses laser light pulses, each in superposition, to deliver a quantum key of encrypted data between sender and recipient. Using specially encoded photons, standard in quantum cryptography, the microsatellite sends quantum keys to ground stations. If anyone attempts to intercept the transmission, the fragile quantum states collapse, and the disturbance is detected and both parties are alerted. This technology currently will allow for future, easier access to quantum keys, where official organization and potentially other users could tap into a quantum-secured channel. It enables sensitive data protection by shifting security dependence away from mathematical complexity, providing defense against current and future threats. Hence, the increasing use of AIoT and breakthroughs in quantum communication bring significant opportunities for future expansion of technologies in space observation, exploration, and global connectivity.

Conclusion

From the launch of the first satellite in 1952 to today's development of AI-integrated systems, it is not contestable that satellites are one of the most complex and essential engineering advancements of the 20th and 21st centuries. Human society and development, from the weather report on the news to GPS would be severely lacking without the development of satellites to help. At the same time, there are many issues to be addressed with the now overwhelming reliance humans have on satellite technology, starting with stuff like bandwidth limitations, space debris, and much more. As humans grow to rely on satellite systems for more than current uses, such issues must be addressed and mitigated in order to prevent future harm.

By Jemima Fong, Sreehaasini Jakkaraju, Fatima Patel, Eleanore Shiner, and Yoana Evgenieva Rekarska

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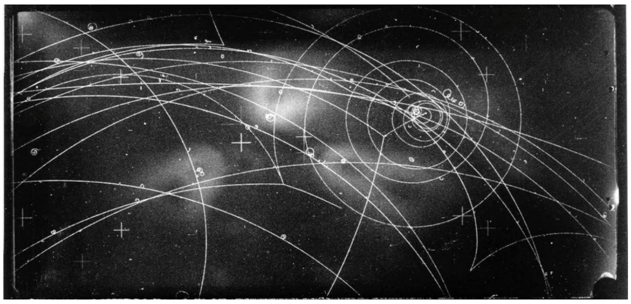

The Effect of Symmetry on the Universe

The laws that govern the universe are derived through the observation of systems and the recognition patterns within them. One such pattern, symmetry, is shown through Noether's theorem, to give rise to the universe's conservation laws. The theorem states that any continuous symmetry produces a corresponding conservation law.

A symmetry is mathematically defined as an action which leaves the overall state of the system unchanged [1]. A continuous symmetry is one in which a system is the same given any size shift in the coordinate system. As a result, Emmy Noether imagined an empty universe in the development of her theory. If a ball were to be propelled forward in this universe, it would continue at a constant velocity as the universe shifts to cancel the motion of the ball and the the forces acting on it would not change. This spatial translation symmetry in the universe gives rise to the law of conservation of momentum [1], [2].

However, our universe is not empty which breaks the spatial symmetry that would have otherwise existed. Einstein discovered this in his theory of general relativity, which describes how the universe curves around objects with mass. And so, if a ball were propelled in this universe, momentum would not be conserved as you can no longer shift the universe to cancel the motion of the ball as the ball no longer moves through a smooth universe which is symmetric in every direction [1], [2].

His theory also predicts an expanding universe, which was shown to be true through the discovery of red-shifted photons. The idea of photon red-shifts means it loses energy by moving through space, which seems to contradict the law of conservation of energy. There are very few particles in space for the photon to collide with, yet energy transfer still takes place. This can be explained by considering the symmetry that produces the law of conservation of energy.

An expanding universe breaks temporal translation symmetry, meaning that the corresponding symmetry of the law of conservation of energy is temporal translation symmetry. On smaller scales time translation symmetry is conserved as we can neglect the difference in the expansion of the universe. Local symmetries like this are why we observe conservation laws without there being a corresponding global symmetry.

The study of symmetries unlocking the physical properties of the universe did not end with Emmy Noether. The cosmic microwave background radiation shows an almost uniform temperature of the universe on large scales which is caused by the uniform expansion of the universe. Galaxies, which are formed out of small quantum fluctuations in an otherwise symmetrical universe, are points where there is a variation from the universal temperature. Thus breaks in the symmetry of the early universe are essential in understanding the current state of the universe.

The nature of dark matter, one of the most fundamental questions about the universe, is being explored through understanding why there is an asymmetry in the standard model. Dark matter makes up approximately 80% of the mass of the known universe and is practically invisible as it interacts only through the force of gravity. This description is similar to that of the theorised sterile neutrino.

Neutrinos and antineutrinos have no charge and differ in their chirality, which is a fundamental property describing the spin preference of the particle and the direction of motion. Neutrinos are expected to have chiral reflections but we have only proven the existence of the left-handed neutrino. Chirality determines whether a particle interacts with the weak nuclear force; it interacts only with left-handed particles and right-handed anti-particles. The right-handed neutrino is sterile as it does not interact with the weak force and only interacts weakly through gravity [3].

The experiments conducted by scientists to determine the existence of sterile neutrinos are disputed as different experiments have shown contradictory results. Neutrinos undergo oscillations where they switch between right- and left-handed neutrinos. Anomalies in these oscillations are what scientists hope to detect [3]. The LSND in Los Alamos and the MiniBooNE experiment both show signs of sterile neutrinos but they were not definitive.

The inability of scientists to prove the existence of sterile neutrinos leaves an asymmetry in the standard model as there are left and right handed baryons and leptons. This could be the basis of future research on the properties of dark matter. This difference in the way neutrinos behave could be the basis for our understanding of the properties of matter and allow us to see more clearly the universe we inhabit.

Symmetry is an easily observable phenomenon in nature. Its presence in a system is significant as it can be used to simplify calculations about the future state of said system and the laws that arise as a result of it, like the law of conservation of energy, are essential in making our understanding of the universe more intuitive.

By Abdirahman Mumin

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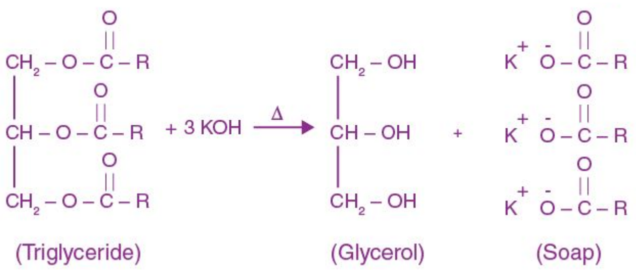
The Mechanisms of Soap Action in Cleaning Processes

On average, people use soap between 7 and 9 times a day [1]. After the COVID-19 pandemic, awareness of hygiene has increased, leading to more consistent handwashing practices. In the United Kingdom, approximately 82% of adults report always washing their hands after using the toilet facilities, while around 34% use hand sanitiser when soap is unavailable [2]. Although the frequency of soap usage is significant, the mechanisms by which soap facilitates cleaning remain unclear for the general public.



Traditionally, soap has been produced through a chemical reaction called saponification. This process involves combining fats or oils with an alkali (lye) and water. The choice of alkali depends on the desired form of soap being made: sodium hydroxide (NaOH) is used for bar soaps, whereas potassium hydroxide (KOH) is used for liquid soaps [3]. When heated, the alkali hydrolyses the fats into glycerol and fatty acid salts, which together constitute the key components of soap [4]. For example, if the triglyceride contains stearic acid (C17H35COOH), the reaction produces potassium stearate, a common soap component [3].

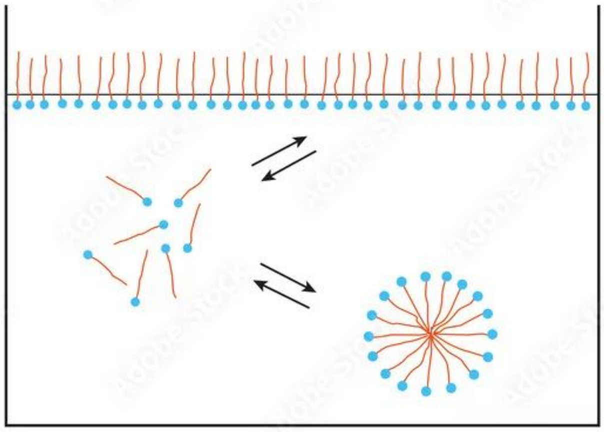
While this method reflects a traditional process used for centuries and documented in ancient civilisations such as the Romans [4], modern soap production involves more complex formulations. Due to technological improvements, additional chemical ingredients are incorporated to enhance properties such as moisturisation, fragrance, and stability [5].

Currently, there are many types of soap, including solid bars, liquid soaps, antibacterial formulations, and exfoliating products. However, all types of soap share the same fundamental purpose: to dislodge dirt from the skin [5]. Shampoos serve a similar function, aiming to cleanse hair by removing accumulated sebum. Both products rely on surface-active agents, also known as surfactants, which are the primary components responsible for the cleaning properties of soaps.

Surfactants are surface-active substances that reduce surface tension at the interface between immiscible substances, such as oil and water [6]. They have a unique molecular structure, consisting of a hydrophilic head and a hydrophobic tail, often described as resembling a tadpole [7]. These properties are responsible for cleaning, foaming, and emulsification. Many surfactants are synthesised from petrochemical sources through reactions such as sulfonation, which involves the addition of sulphur-containing groups. In addition, naturally occurring biosurfactants exist, produced by microorganisms or derived from plant-based sources like palm oil or coconut [7].

The most common surfactants in cleaning products include sodium lauryl sulfate (SLS), ammonium laureth sulfate (ALS), and sodium stearate [6], [7]. Most of these surfactants operate on a similar principle where their amphiphilic nature allows them to accumulate at the interface between water and oil. Surfactants arrange themselves so that the hydrophilic head remains in the water, while the hydrophobic tail extends away from it. When surfactants are added, they disturb the strong attractions of hydrogen bonding, reducing surface tension [8]. This functionality is essential, as it enables the mixing of aqueous and oil-soluble substances, which are fundamental to the cleaning process.

As the concentration of surfactants increases, the molecules begin to cluster together to minimise the exposure of their hydrophobic tails to water. This leads to the formation of spherical structures known as micelles. The concentration at which micelles begin to form is referred to as the critical micelle concentration (CMC) [8].

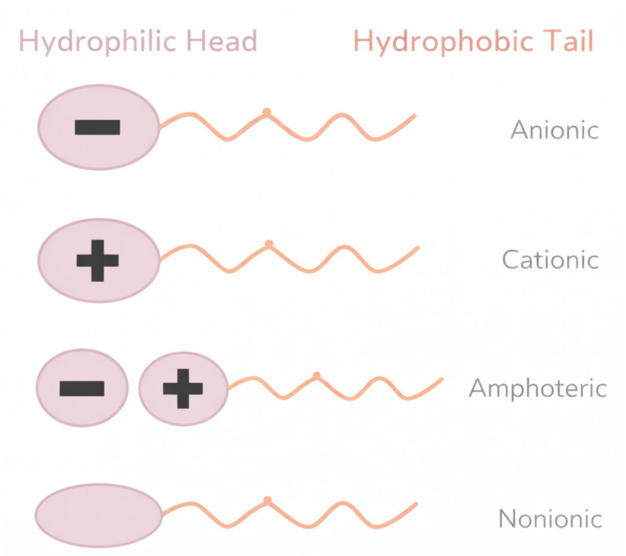


The concept of critical micelle concentration (CMC) is essential in understanding surfactant behaviour. Before reaching CMC, the surface tension strongly decreases as more surfactants are added. After reaching CMC, the surface tension remains relatively consistent, allowing micelles to form. It is crucial to reach a CMC for micelles formation, as insufficient or excessive amounts of surfactants will not result in effective cleaning, as micelles would not form. Therefore the product would not be able to act as a cleanser.

The most common misunderstanding of the critical micelle concentration is that by increasing the number of surfactants present in the solution, the number of micelles will proportionally increase [9]. This only remains true to a certain level, as very high concentrations can reverse the process, leading to breakdown of structures [12].

Micelles are a crucial element in the cleaning process. Oily substances, such as grease and dirt, become trapped within the hydrophobic core of micelles, where the lipophilic tails are aggregated. Since oil and water do not naturally mix, the dirt is attracted to the hydrophobic tails and held within the structure. The outer surface of the micelle is hydrophilic, allowing it to remain suspended in water and be rinsed away [10].

There are four main types of surfactants, each used for different purposes: anionic, cationic, amphoteric, and nonionic surfactants. Anionic surfactants have a negatively charged head, which leads to their cleaning and foaming properties. In contrast, cationic surfactants have a positively charged head, which reduces static electricity and improves the smoothness of a hair. Amphoteric surfactants can either have negative or positive heads depending on the pH of the solution. For example, in acidic conditions amphoteric surfactants will have a positively charged head, but in alkali they will exhibit a negatively charged head. This versatility makes them particularly useful for milder formulations, such as those used in baby or sensitive skin products. Nonionic surfactants have no electric charge, therefore making them suitable for moisturising, as they offer mildness and good compatibility with other ingredients [6], [7]. Depending on the type and required purpose of the soap, different surfactants are used, often in combination with each other to achieve specific formulations.



Although surfactants are considered a primary active ingredient of many commercial soaps, formulations also include other important components such as preservatives, moisturisers and conditioners. For example, sodium hydroxide (lye) is used during the saponification to adjust the pH. Preservatives like sorbic acid help to extend the shelf-life of a product by stopping the growth of mold, yeast or fungi. Additional ingredients are often incorporated to enhance the product performance. The sulfur groups may aid an exfoliation of the dead skin and impurities. To provide moisturising and conditioning, the emollients like *Theobroma cacao seed butter* are included to improve skin softness and elasticity, counter-acting the drying effects of cleansing agents [11].

Although surfactants are in widespread use in a range of applications, acting as detergents, emulsifiers and foaming agents, there are environmental concerns associated with their impacts on sustainability of the ecosystem. The main ethical consideration of using surfactants is the fact that about 60% of the total surfactant produced enters the aquatic environment. This is equivalent to around 7 million tonnes globally at current level of production [12]. Surfactants pose both human and animal risks, as when they contaminate water they increase the solubility of other contaminants, making drinking water toxic. For example, surfactants could potentially react with existing protein in the liver and serum, thus causing long-term disruption of metabolism [13].

Moreover, they destroy aquatic life by reducing the resistance of aquatic biota against environmental stress. The absorption of surfactants by a microorganism can depolarise the microbial cell membrane and decrease the ability of taking in nutrients and oxygen from the water [13].

To conclude, surfactants play a vital role in the cleaning action of soaps through their unique amphiphilic structure. Their ability to reduce surface tension and form micelles allows the effective removal of grease and dirt from surfaces such as skin and hair. While modern soap formulations incorporate a variety of additional components to enhance performance and consumer experience, surfactants remain the primary active-agents responsible for cleaning. However, despite their widespread benefits across product range, the environmental and health concerns highlight the importance of developing more sustainable alternatives, such as biosurfactants.

By Alina Kartašova

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Computational Modeling of Opioid Modification to Reduce Respiratory Depression Risk

Opioids remain among the most effective medicines for managing severe pain. Yet they carry several complications, among them, a well known and fatal risk is respiratory depression [1]. There is currently an ongoing global opioid crisis, in which opioid related fatalities are at an all time high, most of which are caused because opioids disrupt the neural circuits responsible for generating breathing [1].

How Opioids Work

Opioid Induced Respiratory Depression (OIRD) is the leading case of fatal opioid overdose. It is driven by the suppression of a neuron complex responsible for generating breathing rhythm [2], [3]. The most critical center of the breathing process is the pre-botzinger complex, a small cluster of neurons in the brainstem that act as the body's primary respiratory rhythm generator [2], [3]. Under normal conditions, this network produces coordinated bursts of activity that drive inhalation. However, the activation of mu-opioid receptors within this region suppresses excitatory signaling causing overactivation and destabilising the rhythm, leading to apnea caused by the inactivation of breathing [2].

The mu-opioid receptor (mOR) is a G-protein-coupled receptor that plays a dual physiological role [4]. In the pain pathway, activation reduces neuronal excitability and dampens nociceptive transmission, producing analgesia, or pain relief [1]. In the respiratory centers, the same receptor activation suppresses excitatory drive to rhythm-generating neurons, slowing down breathing rate [2], [3]. Within the pre-botzinger complex specifically, mOR activation overactivates arrhythmogenic neurons and makes it harder for them to fire in coordinated bursts [2], [3]. As receptor activation increases, the network transitions from stable rhythmic firing to irregular breathing to complete rhythm collapse [2].

Certain opioids, particularly those who are extremely lipophilic and structurally optimized for receptor binding, are able to easily penetrate fatty tissues and cell membranes and cross the blood brain barrier with extreme speed. This allows opioids to interact with the pre-botzinger complex almost instantaneously [1]. A prominent example is BU72, an experimental mOR superagonist that produces responses much more powerful than classic opioids like morphine [4]. BU72 has an extremely high binding affinity of -11.8 kcal/mol and rapid receptor activation at very low concentrations. Its potency makes it useful for studying receptor structure and signaling dynamics [4], but it also makes it unsuitable for therapeutic use, as it can lead to multiorgan shutdown and the loss of breathing control.

Proposed Solution

If the N-methyl group of BU72 and Morphine are replaced with a polar hydroxyethyl moiety, it will create a pharmacokinetic "polar speed bump." This could increase the polar surface area (PSA), slowing central nervous system (CNS) entry to provide a physical safety buffer for the pre-Botzinger complex while maintaining high binding affinity and analgesic effects.

Methodology

The method to achieve this employs a computational modeling approach to investigate structural modification of opioids to reduce respiratory risk, using simulation programs such as PyRx, PyMol, Avogadro, and PLIP to collect and analyse data. The mu-opioid receptor (MOR) obtained from the Protein Data Bank (PDB) with the ID 5C1M, is an active state receptor [4]. The MOR and Ligand (BU72) were then separated and cleaned, removing unnecessary and redundant atoms and molecule groups, in PyMol. Then, N-substituent modifications were performed in Avogadro, replacing the methyl group with a hydroxyethyl group then performing MMFF94 geometry optimization. These modified molecules, BU72 and Morphine, were run in a simulation in AutoDock Vina via PyRx using 5C1M MOR with an exhaustiveness of 24. Results were analyzed using PLIP (v2.4.0) for interaction mapping and bond distance validation.

Results Analysis

Molecular docking simulations were performed to evaluate how N-substituent modification influenced ligand binding at the MOR. The original binding affinity of ligand BU72 was -11.8 kcal/mol. Following substitution of the N-methyl group with a hydroxylethyl moiety, the modified ligand produced a moderately elevated binding affinity of -12.0 kcal/mol. Notably, a new hydrogen bond interaction formed with LYS303, with a shorter hydrogen bond distance of 2.61 A.

A similar trend was found in the morphine modifications. The original morphine had a binding affinity of -6.7 kcal/mol. After modification with the hydroxyethyl group, the predicted binding affinity increased to -8.1 kcal/mol, and the hydrogen bond with ASP147 strengthened to a shorter distance of 2.05 A.

Across both modification frameworks, the hydroxyethyl substitution improved predicted receptor binding while increasing the Polar Surface Area. This data suggests that increasing ligand polarity does not necessarily compromise receptor interaction strength.

Overall, the docking results support the feasibility of modifying opioid ligands to retain strong receptor engagement while increasing polarity. These findings provide computational evidence for a strategy aimed at modulating drug delivery dynamics without sacrificing receptor binding capability.

Conclusion

Opioid safety may depend not only on potency, but on the temporal dynamics of neural inhibition [1], [2]. By utilizing a computational approach, we deducted that increasing ligand polarity could slow CNS entry while maintaining receptor affinity. These modifications may help prevent the rapid inhibitory overload that causes respiratory depression. While experimental validation is required, these findings support a broader hypothesis: protecting neural network stability may be as important as limiting receptor activation.

By Alper Cebel

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Hydration and Its Effects on Focus in High School Students

1. Introduction

Water is crucial for nearly every biological function in the human body. This includes thermoregulation, digestion, transport, and joint lubrication [1]. Although it is difficult to prioritize one function of water over another, hydration is essential for cognitive function. Forming the basis for blood, water is necessary for transportation throughout the body [2]. Without blood, and by association, water, oxygen and other nutrients cannot reach the brain. Moreover, proper hydration helps neurons transmit and process electrical information [3]. This is important for cognitive function. Studies have indicated that dehydration is widespread and common among school-aged children [1]-[4]. This can make it difficult for adolescents to navigate their daily tasks and succeed in environments that require high levels of focus [4].

Studies using the military population—and later the general population—have shown that dehydration can negatively impact cognitive function. When measuring sustained attention, performance deficits were observed, increasing with the severity of dehydration [5]. This is important to address because children have been found to be at higher risk of voluntary dehydration, which suggests that adolescents may similarly be vulnerable [6]. Considering that high school students' brains are still developing and that their schedules are often irregular, this topic warrants further investigation. However, research focusing specifically on teenagers aged 15 to 18 remains limited.

This study aims to address the gap by exploring whether there is a significant relationship between hydration levels and self-reported focus among high school students. By surveying adolescents' daily water intake and concentration levels, this research seeks to understand how the simple lifestyle change of drinking more water could impact mental clarity. We hypothesize that students who consume more water during the day will self-report higher levels of concentration compared to those who consume less.

2. Methods

2.1 Participants

This study involved 13 high school students, ages 15-18. These participants were recruited from the researcher's network of colleagues as well as voluntary online responses from anonymous individuals.

2.2 Procedure

Students completed a form about their water intake for that day. They responded with their estimated water intake in ounces, a self-rated level of focus on a scale of 1-10 with 1 being not focused at all and 10 being very focused, and any optional notes on other factors that may have influenced focus.

2.3 Data Analysis

Once the responses were collected, focus scores were averaged and compared across different hydration levels. Graphs, along with the use of averages, were used to identify any patterns.

3. Results

3.1 Water Intake vs Focus

Thirteen participants reported their estimated water intake and focus levels for the day. Water intake ranged from 4 oz to 87 oz, while focus scores ranged from 3 to 8 on a 10-point scale. Figure 1 shows each participant's approximate water intake in ounces and their corresponding focus rating on a 10-point scale. Conducting a test for correlation gives a correlation coefficient of 0.2864. The scatterplot showcases this weak to moderate positive trend between water intake and focus. Participants who drank over 60 oz of water typically reported focus scores of 7-8, with the average being 7.5. Participants who drank between 30-60 oz of water reported an average focus score of 7. Participants who drank under 30 oz of water reported focus scores of 3-6, with an average focus score of 5.4. Of the participants, approximately 31% consumed an adequate amount of water between 64-88 oz. Approximately 85% of participants reported an above average focus score (5 or higher).

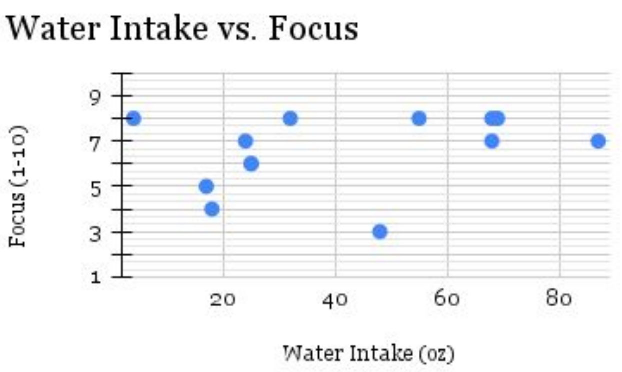

Figure 1.

3.2 Outlying Factors Affecting Focus

Many participants noted other variables that could influence their concentration. Sleep deprivation was mentioned in over half of responses, often citing 5-6 hours of rest. Outside variables included ADHD, illness (e.g. colds, ear infections), caffeine and physical fatigue from exercise

Although the trend is clear, external factors make it difficult to isolate water intake as the sole influence on focus. Even with these factors, the overall direction of the data supports a positive relationship.

4. Discussion and Conclusions

The results show a general positive trend: the participants who reported consuming higher amounts of water tended to report higher levels of focus. Those with daily intakes of 64 ounces or more reported an average focus score of 7.25, whilst participants who had a daily intake of less than 64 ounces had an average focus score of 5.8.

These results align with existing research that used adults to link dehydration to lower cognitive function [3]. The sample size of high school students was small; however, the upward trend between water intake and focus helps support the hypothesis that hydration plays a meaningful role in adolescent concentration.

Of the other variables that may have played a role in the levels of self-reported focus, sleep deprivation was the most frequently mentioned factor, with more than half of the participants citing it. It is important to note that many participants who cited outside factors (e.g., fatigue, illness) had high focus levels. This may be caused by the fact that those participants reported drinking adequate amounts of water.

Due to the short survey duration and limited number of participants, these results cannot establish causation. Self-reporting may introduce possible inaccuracies in estimating water intake and focus levels. Future research with a larger and more diverse adolescent population, as well as objective hydration measurements (e.g., urine osmolality), and controlled conditions would help clarify the direct relationship between adolescent focus and water consumption.

By Amelia Diemert

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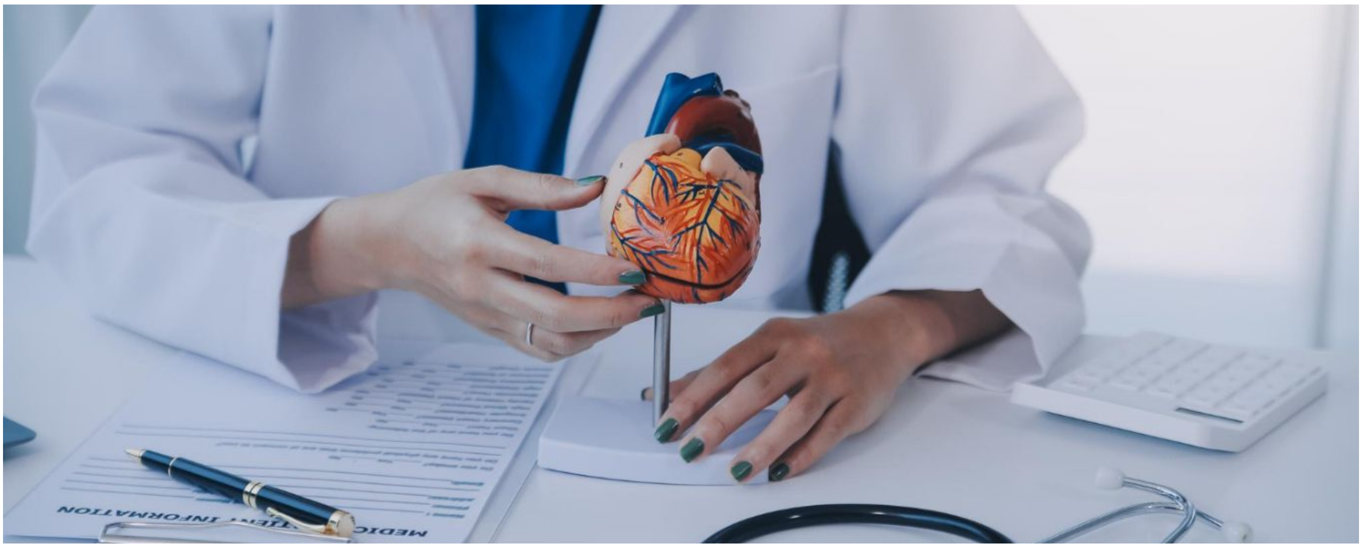

How Access to Cardiovascular Treatment Should Be Determined

In 2026, Cardiovascular disease is the leading cause of death globally which can be linked to a rapidly aging population, high rates of obesity, and widespread lifestyle-related risk factors, with an annual death toll of an estimated 17.9 million [1]. Cardiovascular issues also cause economic burdens. 7.5 billion hours of unpaid care by relatives were provided to people whose needs were directly attributable to cardiovascular disease, costing the EU €79 billion [2], emphasizing the need for global access to cardiac treatment.

However, cardiovascular treatment is expensive. For example, cardiovascular disease treatment costs the EU's health and social care systems €155 billion, which is 11% of total health and social care spending [2]. Governments cannot provide unlimited access to the advanced cardiac care people need, raising ethical questions about compromises between economic viability, clinical need and likelihood of success. Prioritisation should primarily reflect clinical need within economic limits, and while likelihood of success should guide individual decisions, it does not justify institutional exclusion of people that stifles innovation.

Firstly, economic reality and viability must be considered as healthcare resources are finite. NHS England received a budget of £153 billion in 2022 to serve the English population of 57 million [3], [4]. This equates to roughly £2,700 per person per year which could be a limiting factor in how the NHS decides treatment options. An example of an expensive treatment is a heart transplant as an average heart transplant in the UK costs £30,758 with around 200 heart transplants being done in the UK every year [5].

In order to balance budget with patient outcome, healthcare systems use a metric called a Quality-Adjusted Life Year (QALY) [6]. QALYs balance expected years of life left, with quality of life such as freedom from pain using a quantitative scale. These QALY assessments are used by the NHS and National Institute for Health and Care Excellence (NICE) to determine the value of new therapies within budget [7]. NICE aims to reduce health inequalities, and support innovation through transparent and objective allocation of limited financial resources. Currently, the NHS will pay between £20,000 and £30,000 per QALY [7], and is a highly influential number impacting treatment options and outcomes.

The effect of QALYs is demonstrated by the reduced use of Left ventricular assist devices (LVADs). Using a Markov model, LVADs were calculated to add 2.78 QALYs and are used for people with advanced heart failure, especially in cases where heart transplant is not possible [8]. LVADs are not used in the UK as a long term solution due to the high cost of £54,748 per QALY surpassing the £30,000 limit [8]. This means some people will be unable to be provided with necessary treatment, which may result in shorter lifespan.

Medical need is also crucial to consider, though it can be very subjective as it lacks a standardised definition. It can include many factors such as urgency of survival, potential years gained, or quality of life improvements [10]. Since medical need is not neutral it is made vulnerable to manipulation by powerful groups. Davies [11] argues that if medical need is vague, then well-resourced groups may categorise their claims as medical need and poorly resourced groups may be neglected, losing fairness for patients. For example, many advanced cardiac procedures such as transcatheter aortic valve implantations (TAVIs) often benefit older populations, as the average age of a TAVI patient is between 75 and 80 [12]. Older populations are often wealthier and have more senior roles in the healthcare sector and will have the bias to categorise treatments that benefit their demographic as being of higher medical need. This reduces their immediate mortality risk but may divert funds away from younger patients with long term cardiovascular issues.

Therefore, increasingly common issues in young adults, such as hypertension, that do not cause immediate death, but raise risk of cardiac issues later in life, could be disregarded by medical systems as being in less need [13]. Prioritising immediate survival over long-term prevention or treating chronic issues is not just a medical decision, but also affected by political factors. This inequality in influence in institutional decision making could affect historically marginalised groups such as women. Until recently, there has been a lack of female representation in clinical trials leading to inadequate diagnoses. This has happened through attributing symptoms to hormonal factors without sufficient investigation, causing female cardiovascular health to have improved significantly less than in males [14]. In order to prevent bias and discrimination, medical need should be heavily considered in an institutionally standardised and clearly defined manner.

Finally, likelihood of success is an important factor to be considered. Although it is vital to maximise survival probabilities for patient treatment, overprioritising this in clinical decisions risks abandoning patients with difficult conditions. For example, extracorporeal membrane oxygenation (ECMO) can be used to treat patients suffering severe cardiogenic shock, which is when there is a sudden and profound reduction in cardiac output; however, it has a high mortality rate ranging between 30% and 70%. In the US, an estimated 40,000 to 50,000 people go into cardiogenic shock annually [16]. If allocation is driven by predicted survival, critically ill patients may be denied ECMO, reducing chance of survival. Despite the treatment having high mortality rates, the difference in survival rates is around 10-30 percentage points [22], which represents thousands of lives that could have been otherwise saved.

Without risk and investment, innovation stalls, limiting future QALY gains. An example of this is the first human heart transplant in 1967 performed by Christiaan Barnard [17]. It was initially successful, but unfortunately the patient died 18 days later due to pneumonia because his immune system had been weakened by immunosuppressant drugs that he had taken to prevent rejection [17]. At the time, true success rates for heart transplantation were low and if only the likelihood of success was considered, transplantation would have been abandoned. However, heart transplants continued and prognosis improved slowly over time. In 1968, Barnard gave another transplant to another patient called Philip Blaiberg, who managed to live 19 months, [18] demonstrating improvement. Today, heart transplants are largely successful with an average lifespan of 13 years post transplantation [19], [21]. This can be attributed to refining of techniques and the development of safer immunosuppressant drugs such as the discovery of cyclosporine in 1971 [20]. This elucidates that tolerating a low chance of success in treatments like heart transplants, can allow for improvement.

To conclude, medical need should be the main factor in considering access to cardiovascular treatment within economic boundaries to ensure the best treatment for most patients.

This will ensure that innovation is promoted ensuring we give the best care to patients today, whilst also having better technologies and the money to treat the patients of tomorrow.

By Andrew Caicedo Ortiz

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Intersections of AI: Revolutionising Perinatal Care

1.0 Intro

Perinatal care refers to the care the mother and baby receive during the gestational period, covering both antenatal (before birth) and postnatal (after birth) care [1]. As part of perinatal care, mothers are invited to a number of screening and diagnostic tests.

These screening tests are used as a way of identifying mothers with a higher chance of a health problem in order to allow them to get earlier, more effective treatment. In terms of antenatal scans, they include blood tests to check for HIV, hepatitis B and syphilis and also screening for Down's syndrome, Edwards' syndrome, and Patau's syndrome [2].

This influx of information must be interpreted quickly and accurately by clinicians; however, there are still numerous preventable complications such as preterm birth and preeclampsia that remain difficult to identify. As a result, AI is increasingly being used to enhance risk prediction, diagnostic accuracy, and operational efficiency across the perinatal continuum [3]. This supports extensive personalised care and provides a more proactive approach to maternal and newborn health.

2.0 Urgency Of Improving Perinatal Care

According to the World Health Organisation (WHO), in 2023, approximately 260,000 women died from preventable causes related to pregnancy and childbirth. This is significantly lower than in 2000, when there were an estimated 443,000 maternal deaths [4]. Whilst there are a multitude of factors to take into account, the growing use of AI for diagnoses coincides with this great decrease in mortality rate, accentuating the benefits of AI and why it should be prioritised in healthcare policies and innovations. Despite these advancements in medicine, health risks during pregnancy are still alarmingly high, particularly in low and middle income countries [5].

3.0 AI Initiatives

3.1 Bloomlife

Preterm birth is a leading cause of neonatal morbidity and mortality; however, with new machine learning models, through the collection of standard clinical data such as C reactive protein, and BMI, this technology can predict preterm delivery with over 80% accuracy [6]. This allows doctors to intervene earlier, increase surveillance, and plan for delivery at a specialised centre. Whilst high-tech machines may appear to drive the disparities in healthcare further apart, these models have inspired AI-driven wearable devices, like Penders' Bloomlife [7], that detect foetal movement, predict labour onset, and predict preterm birth, all remotely. The facilitation of continuous remote tracking of maternal and foetal health improves equity, especially in Low income countries where specialists are rare and distance is one of the greatest barriers to care [6].

Fig. 1: Penders' Bloomlife device worn across the stomach with data tracked on the phone.

3.2 Diagnosis of FGR

Foetal growth restriction (FGR) is the underdevelopment of the foetal potential to grow in utero which leads to further difficulties at birth. According to WHO, over 20 million newborns have a birth weight of less than 2,500g, which is defined as low birth weight (LBW) [4]. A low birth weight is linked to developmental delays such as slower language acquisition and impaired intellectual functioning. A solution to this issue is through the use of AI. The way AI has been implemented so far is through supervised learning algorithms that are trained on labelled data sets. These algorithms can then classify whether a foetus is at risk of FGR based on a few input features, including maternal characteristics and foetal measurements. Zhang's contribution of the image quality control allows clinicians to accurately identify anatomical structures in sonographic images, enabling for a more in-depth analysis of the foetal biometry which can then identify if there are any concerns [8]. This once time-consuming process has been reduced to less than a second, allowing doctors to dedicate more time for the human aspects of medicine such as decision-making, empathy, and complex problem solving [6].

4.0 Limitations of AI

Despite the promising nature of AI, its integration into modern healthcare must not replace a doctor's ability to think critically. For example, IBM Watson was marketed as an AI oncologist that was said to be able to recommend personalised cancer treatments, leading to numerous hospitals investing millions into the programme. However, upon further research it was found to be faulty, often providing unsafe and irrelevant recommendations due to its lack of patient data [9]. Furthermore, the lack of clinician oversight in its early deployment stages meant that problems went unnoticed. This emphasises the importance of not relying solely on AI but rather using it to support a doctor's treatment.

5.0 Conclusion

Overall, AI has been used across multiple sectors of healthcare to improve patient care and diagnostic accuracy. It is particularly useful in perinatal care as it improves the current screening systems by managing mass data and finding patterns within seconds. Methods like Bloomlife greatly enhance the experience of pregnancy and improve the chance of survival for both the mother and the foetus, particularly in rural and disconnected areas. Whilst AI tools have been proved increasingly beneficial to the healthcare system, a doctor must be able to discern whether the provided information from these tools are accurate. Despite being programmed to identify and diagnose problems, the final say in treatment remains within a clinician's responsibility and doctors must not use this technology as an excuse to slacken, but rather to supplement their current knowledge and also have more time to foster a deeper, more personal relationship with each patient.

By Anna Caniparu

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Artificial Intelligence's Use in Supercell Tornado Detection

In recent years artificial intelligence has been integrated into many systems used in everyday life, and some scientists have started to test its potential uses for weather data analysis [1], [2]. AI's ability to be trained for specific scenarios indicates a high aptitude for use in science, specifically in analyzing data and finding patterns [3], [4].

Meteorologists have potentially found an impactful use for AI in the field of severe weather prediction. Researchers at Georgia Tech and MIT have started testing the potential of AI in prediction and research of supercell tornadoes through its data analysis abilities [3], [4].

Supercell tornadoes are formed from a supercell storm, a storm containing a mesocyclone. A mesocyclone is the presence of a large rotating column of air with vertical wind shear. Mesocyclones are caused by temperature changes in the layers of air that form when high and low pressure fronts collide, creating friction from the upwards motion of warm air [4], [5], [6].

Tornadoes are extremely difficult to predict because the cause of their formations are not yet understood. Not all mesocyclones produce tornadoes, and one supercell storm may produce a tornado but a nearly identical storm next to it will not [4]. Consequently, forecasters often err on the side of caution and issue warnings [4], [7]. More than 70% of tornado warnings issued never produce a tornado. These false alarms cause distrust in the communities. Many people disregard the warnings and do not make it to safety in time [3], [4].

The Lincoln Laboratory at Massachusetts Institute of Technology (MIT) is attempting to develop an AI based system that would have the capability to accurately predict supercell tornadoes before they form. With the release of a new large dataset called TorNet, they saw new potential to find what conditions are required to produce a tornado and improve the tornado warning systems to be faster and more accurate. TorNet is a collection of radar images of storms curated by Lincoln Laboratory researchers that has now been made open source [4].

The image dataset fed to the machine learning AI contained more than 200,000 radar images. 13,587 of these images depicted tornadoes, while the rest were either severe storms or false alarm storms. The researchers chose to use AI systems that applied deep learning, a form of machine learning that excels at processing visual data such as the radar images from TorNet. Researchers chose systems that utilized deep learning to see if AI could rediscover what scientists look for in supercells and potentially identify new things that are not typically looked for. The results have been promising, the algorithm correctly classified 50% or weaker EF1 tornadoes and over 85% of EF2 or higher [4].

Weather radar is the primary tool used in forecasting, and is the system used for determining whether to issue a tornado warning or not [3], [7]. This is problematic considering tornadoes form too low for radars to capture, making them invisible on radar [3]. Topographic features can limit radar visibility as well, making it difficult to see the bottoms of storms [1]. Electromagnetic interference also affects radar results, blocking them or giving a false positive [3]. The time required for radar systems to update their views can cut into the valuable time between a warning and a tornado to touchdown [3], [4].

Scientists at Georgia Tech have taken a different approach to detecting supercell tornadoes. Instead of using a radar system, they opted to train their AI with data from geostationary satellites and a ground based lightning mapping system [3]. By using the geostationary satellite data, they avoid the limitations of radar and have a much wider view of the storms. Using this technique, it is possible to evaluate up to 40 different parameters to analyze for any correlation to tornado formation [3].

One of the factors researchers at Georgia Tech are also considering is patterns of lightning. Recorded radio frequency emissions by the array to study lightning flashes can be analyzed by AI for any correlation between "jumps" and "dives" in lightning frequency, and severe storm development [3].

The ground based lightning mapping array, developed by John Trostel, consists of 12 ground stations. These stations record the electromagnetic energy produced by lightning with timing and location information. The data is then used to make a map of the lightning in the area, also including if it interacted with the ground or stayed in the clouds. This phenomenon of lighting interaction is being studied by many scientists across the world and while a correlation has not been established yet, scientists are making progress [3].

So far researchers at Georgia Tech have trained their artificial intelligence system on data from 40 storms resulting in 62 tornadoes, all in Georgia [3].

In the last few decades, global warming has been changing the patterns of severe weather outbursts that cause supercell tornadoes and making extreme weather even more severe [1], [2], [6]. The effects present as less days developing tornadoes per year, but on the days that produce supercell tornadoes, there are more tornadoes produced from the same storm system, and the tornadoes are more volatile [6].

While the futures of these systems look promising, artificial intelligence has been proven to have issues making accurate predictions for weather events that lie outside the training data [1], [2], [4]. One team at Yale conducted a study to test the implications of this limitation on weather forecasting. The study concluded that AI systems frequently underestimated weather events when not trained with data that demonstrates an event of the same scale [4]. Yale scientists fed an AI years of weather data excluding any data from hurricanes stronger than a category 2. When the AI was given conditions that would lead to a category 5 hurricane and asked to make a forecast, the AI was only able to predict a category 2 hurricane [1].

AI's inability to predict extremes makes many scientists question its future in weather forecasting, due to the danger that comes with underpredicting severe weather [1], [4]. One sentiment shared by researchers in many of the studies evaluated was that these AI systems are not meant to replace scientists, but instead to work alongside scientists and help them learn how to accurately predict tornadoes [1], [2], [3].

By Anna Eisinger

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Myopia and Its Lesser Known Solutions

Myopia, also known as nearsightedness, affects an estimated 34% of people as of 2020 [1]. The condition occurs when the axial length (AL) of the eye measured from the front to the back of the eyeball, is stretched. As a result, the cornea and the lens, structures in the eye that focus images by refracting light, will cause the retina to send blurry images to the brain [2].

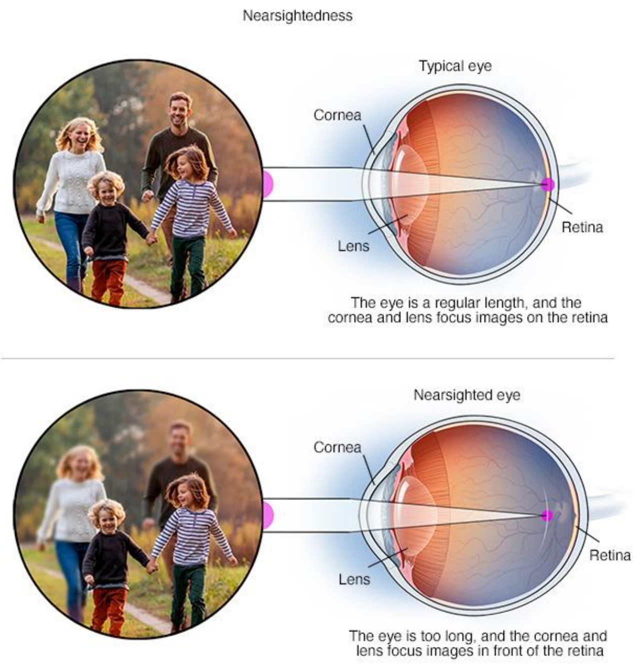

Fig. 1. Differences in myopic and nonmyopic eyes.

Eyeglasses and daytime contact lenses are the most popular options for correcting myopia. However, lesser known solutions such as orthokeratology (Ortho-K) and repeated low-level red light therapy (RLRL) offer benefits.

Orthokeratology

Soft daytime contact lenses are the most popular and well known option for contact lenses. On the other hand, only 1.2% of all contact lens fittings are orthokeratology lenses [3]. Ortho-K lenses are specially designed lenses that temporarily reshape the cornea during nighttime wear.

Since Ortho-K lenses are custom made, a scan of the patient's cornea is required to design the lenses, typically achieved using corneal topography (CT) [4]. During this process, the patient sits in front of a CT device, which scans the eyeball by projecting a series of concentric rings onto the cornea. The rings, also known as "mires", allow CT scans to be interpreted. For example, the cornea has steeper curvature in areas where the mires are closer together [5].

Ortho-K lenses press on a very thin layer of tear film in front of the cornea [6]. This exerts a pressure on the top tissue layer of the cornea, known as the epithelium. The lenses squeeze the epithelium fluid from the center to the sides, temporarily reshaping the cornea [6], [7].

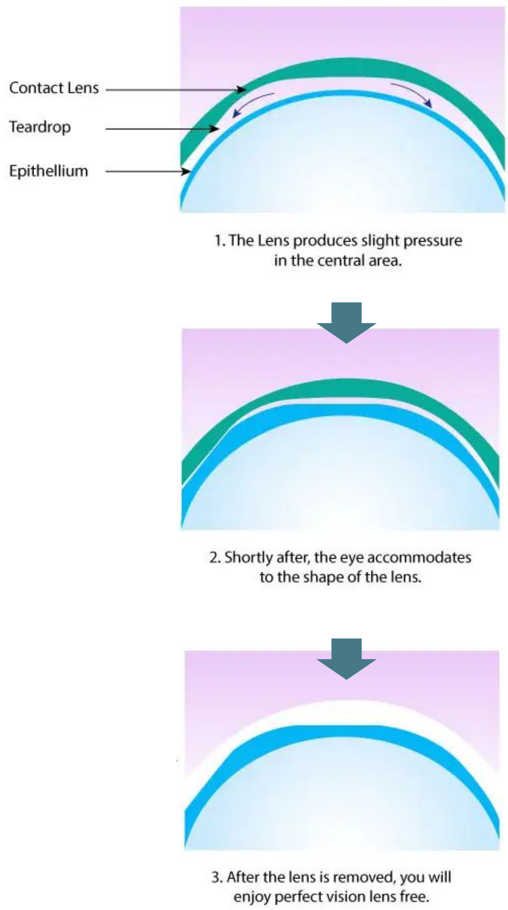

Fig. 2. The contact lenses press on the tear film and epithelium, causing the cornea to be reshaped.

An additional reason for choosing Ortho-K lenses is its ability to not only correct myopia but also slow progression. The Stabilizing Myopia by Accelerating Reshaping Technique (SMART) study found that myopia advanced at a significantly faster rate in children wearing soft daytime contacts than in children wearing Ortho-K lenses [8]. The results were quantified using diopters, a unit of measurement that evaluates the focusing length required for a pair of lenses. A negative diopter is for myopia, while a positive diopter is for farsightedness. A diopter of a greater magnitude indicates a worse vision and a stronger prescription on the corrective lenses [9].

Over a three year period, the SMART Study discovered that the mean change in myopia for the daytime contacts group was -1.03 ±0.58 diopters versus only -0.13±0.62 diopters for the Ortho-K group [8]. This difference of over 0.5 diopters demonstrates the Ortho-K lenses' ability to slow myopia growth.

However, one drawback of Ortho-K lenses is its impermanence. Ortho-K lenses must be consistently worn every night, or the cornea will return to its original shape due to a lack of pressure [4].

Repeated Low-Level Red-Light Therapy

Repeated low-level red-light therapy is a relatively new form of myopia control for children and adolescents. One advantage of RLRL is ease of use. Users look into the device twice a day for three minutes each day [10]. Despite its novelty, over 20 studies about RLRL have been conducted in China as of 2024. All suggest that it slows progression and even delays the onset of myopia for pre-myopic children [10]. For example, in a study with 192 children between the ages of 6 and 16, the RLRL group experienced a mean AL change of -0.06 mm, whereas the control group had a mean AL change of 0.34 mm, and 53.3% of the RLRL group were still experiencing an axial shortening of over 0.05 mm 12 months later [11].

RLRL stimulates photoreceptors in the eye, which slows the growth of AL [12]. The high wavelength and low frequency of the red light inhibit myopia onset and progression [12].

Although RLRL seems like a viable solution for myopic adolescents, there are still setbacks to consider. Not enough research has been conducted on the long-term safety of the treatment. Overexposure to red light energy has been a cause of concern [10].

Conclusion

Orthokeratology and repeated low-level red-light therapy are two of the lesser known solutions to myopia. In contrast to normal glasses or daytime contacts, they offer advantages such as slowing myopic progression. As myopia is one of the most common eye disorders, educating the public about these lesser known technologies will have countless positive impacts.

By Audrey Wang

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AI in The Battle Against Email Spam

Digital Spam: A Brief Outline

Unwanted advertising and cyberattacks have existed since early in the internet's existence. The term 'spam' was first used to refer jokingly to accidental unwanted posts on Usenet newsgroup network in 1993 [1]. It can be defined as the attempt to abuse or manipulate a techno-social system by producing and injecting unsolicited or undesired content aimed at steering the behavior of humans or the system itself, for the advantage of the spammer(s) [2]. Spammers often aim to leave victims vulnerable to phishing and other cyber-attacks that could lead to financial loss, identity theft, or worse.

Email spam is particularly prevalent since emails are convenient, cheap, and considered pivotal to everyday tasks. Being flooded with junk mail can leave victims vulnerable to phishing and other cyber-attacks that could lead to financial loss, identity theft, or worse. Additionally, spam poses a problem for companies providing email services since they are then at risk of losing a valuable consumer base.

The Search for Solutions

Many attempts have been made over the last two decades to reduce the advent of spam mail in our personal inboxes, including white and black domain lists, rule based filtering, and Bayesian statistical analysis. White and black domain lists were used to keep track of what sender addresses were legitimate (ham) or spam. This allowed all mail from the spam address to be blocked from the inbox [3]. Rule based filtering used a predefined set of rules to search emails for common features of spam, for example suspicious URLs or misspelled text [4]. Finally, Bayesian statistical analysis uses Bayes Rule, a statistical theorem that can calculate the probability of an event. It serves as a foundation for more modern spam filtering techniques by helping machines determine the probability that an email is spam [5].

Older methods of spam filtering, including the above, had serious restrictions. They often relied on known spam patterns or structures and could not cope with any advancements to spam attacks in real time. As a result, spam was often undetected and allowed into the inbox (false negatives), or legitimate mail was flagged as spam (false positives).

Understanding Natural Language Processing (NLPs) And Machine Learning Algorithms

Natural language processing represents a multifaceted domain within artificial intelligence (AI) and computational linguistics. The field is dedicated to equipping computers with the capability to understand and manipulate human language in various forms, including written text, spoken language, and gestures [6]. NLPs are able to form contextual relationships between words and sentences by breaking down emails into smaller units called tokens and using transformer architecture; a design layout which allows NLP models to form links between words in text even when they are not next to each other [7]. Thus, allowing them to identify spam not only based on the contents of the email but also on the emotions and subtleties it tries to convey.

Additionally, tokenization also allows NLPs to detect emojis and extract meaning from their position in the email, allowing them to better understand semantic relationships between words. This makes NLP models useful for weighing tokens because they can assign scores to each token depending on its meaning in the email.

Furthermore, machine learning algorithms enable spam filtering models to improve their performance over time without explicit programming. Some examples of machine learning algorithms are Support Vector Classifier (SVC), Random Forest, Neural Network, Naive Bayes, and Bidirectional Encoder Representations from Transformers (BERT). This means NLP-driven filters are adaptable and could be expanded and used in different settings as was done at Kaggle, a data science company [8].

Within the realm of email spam detection the Support Vector Classification algorithm was used to distinguish patterns in features extracted from an email, weigh the features by combining the emails' token scores and determine if the email was suspicious (denoted as 1) or not suspicious (denoted as 0) [9]. This particular algorithm resulted in 98.65% accuracy, which surpassed many traditional spam detection approaches. Due to their efficiency, NLPs and Machine Learning algorithms are used in email applications like Gmail, yahoo and outlook.

Limitations And Obstacles: The Moving Goal Post

The utilization of NLPs and machine learning models is still resource intensive. As a result, underrepresented situations and demographics in training data may lead to biases in performance when in diverse real-world scenarios [10]. For example, NLP models trained on a single language or a limited set of languages may not perform effectively on phishing emails in other languages. Detecting phishing emails in multilingual environments requires training the model on diverse language data. This means ensuring that it can handle variations in syntax, grammar, and tone across languages. Thus, expanding each models' use in non english environments would require exposing it to large datasets in different languages, which often are not available due to limited technology in disadvantaged areas where other languages are spoken.

Conclusion

To conclude, spam filtering has been a problem from the beginning of the internet with many solutions having been proposed from simple domain lists to more complex algorithms. However, the arrival of AI has brought with it new challenges and solutions to how spam is handled in industry. Natural Language processing and machine learning algorithms are being utilized for semantic analysis and automatic filtering reducing the number of victims of email based spam attacks. Additionally, as attackers continue to evolve their tactics, NLP-based systems must constantly adapt to keep up with these changes, making continuous model retraining and fine-tuning necessary to stay effective [11].

By Choolwe Munsanje

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Autoimmunity in Women

Autoimmune conditions occur when the immune system is unable to differentiate between the body's healthy tissues and foreign antigens. This leads to the immune system's defenses attacking its own cells, the body's immune response then responds to this with a myriad of symptoms such as tissue damage, inflammation, and organ dysfunction [1].

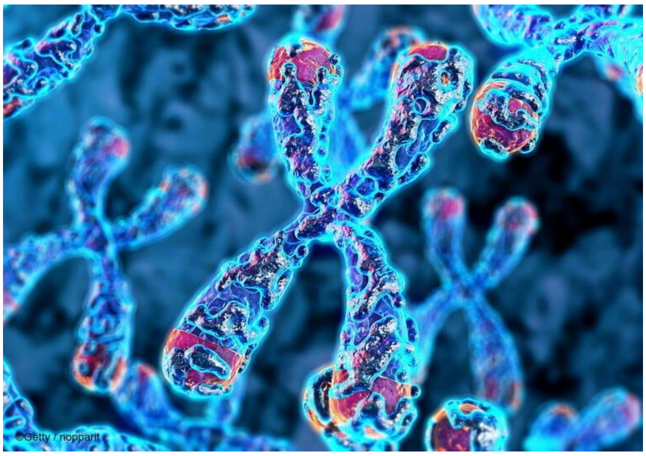
Autoimmune conditions have two main categories, systemic and organ specific. Systemic diseases involve multiorgan failure, due to the wider spread of immune dysregulation. Whilst organ-specific, much like the name, focuses primarily on a singular organ or gland. As well as thus polyautoimmunity can occur, polyautoimmunity is the co-existence of two or more autoimmune conditions. This is independent of the specific autoimmune condition the individual has.

Research has shown that there are over 100 different autoimmune conditions discovered so far, with the most prevalent systemic being rheumatoid arthritis (RA). Whilst the cause of RA is not fully understood, it is thought to be a destructive joint disease, affecting people of all ages, often developed in the later stages of life (late onset). As RA primarily affects the membrane of joints, its clinical manifestation is stiffness, tenderness, inflammation, and loss of mobility. There is no cure for it, but certain factors are thought to increase the likelihood of developing the condition. A positive correlation between pest control workers and RA was shown, suggesting the risk increases through the usage of pesticides and chemical fertilisers.

Yet it must be understood that RA is a much more common phenomena in females compared to males, being 2 to 3 times more frequent, with flare ups worsening during pregnancy. Indicating that reproductive factors and sex hormones are amongst the most influential factors of this disease [2].

As the body contains hundreds of cells, there are many non-life-threatening autoimmune conditions, some of which, when recognised as having foreign antigens, will not cause adverse effects. An example is Vitiligo, it is characterised through white patches of skin, occurring when the skin has lost functional pigment producing-cells known as melanocytes – this makes it an organ-specific disease. Vitiligo is a multifactorial condition, which means it combines genetics, environmental triggers, and each body's autoimmune response. Vitiligo means that melanocytes are more susceptible to oxidative stress. This is caused by an imbalance between production of oxygen reactive species and the ability of the biological systems to detoxify these products. Environmental factors, such as UV radiation, can contribute to increasing the oxygen reactive species production. Thus activating the unfolded protein response, initiating several inflammatory responses through interleukins. Even though this condition does not present as life threatening, it has a significant effect on people's quality of life: decreasing self-esteem, and increasing the risk of sunburn and skin cancer [3], [4].

Several factors cause an increased prevalence of autoimmunity in women. Men and women are both born with 23 pairs of chromosomes; however, the sex chromosome pair differs with XY for men and XX for women. The X chromosome is significantly larger than the Y chromosome and contains up to 900 genes providing information for proteins. A large number of these proteins code for a majority amount of immune related responses [1]. Thus, as women have the XX chromosome pair, it means that they have a higher likelihood of developing an autoimmune condition.



In addition to this, a process called X inactivation occurs in early embryo development. This is where within the XX, the X from the mother is activated, whilst the X from the father is inactivated or vice versa [5]. This means that the X that is inactivated, causes a rise in polymorphic antigens. Even though the antigens originate from the body, the body recognises them as foreign, eliciting an immune response, and causing the body to attack itself due to its own genetic variation [1].

Genetics alone show the increased likelihood of women developing an autoimmune condition; however, another factor that seems to differ from men is hormone production. A majority of women undergo 3 prevalent hormone shifts: puberty, pregnancy, and menopause. Within these biological processes the levels of progesterone and oestrogen fluctuate. With progesterone shifting the body's immune system away from producing antibodies to attacking self-cells. Whilst the latter activates B-cells, which in turn produce antibodies, which will attack pathogens, or in this case self-cells [6].

Androgens such as testosterone, which are produced at a lesser concentration in women, are considered to be immunosuppressants. This is as they decrease immune responses, the possibility that this is the reason that men are less likely to develop an autoimmune condition [6]. Further research has also shown that men who experience decreases in androgens develop or have an increased likelihood of developing Rheumatoid Arthritis [7]. This implies that the androgen testosterone provides an immunosuppressive effect upon the body cells; useful in preventative measures concerning autoimmunity. Yet this hormone may provide adverse effects in immunity when in regards to cancer or toxins.

A higher prevalence of autoimmune conditions are found in women, regardless of their range in symptoms and quality of life. This is due to several factors, most commonly hormonal fluctuations throughout life and a genetic predisposition caused by two X chromosomes. This highlights how our sex seems to be a determining factor in the development of autoimmunity, as well as providing an explanation behind its prevalence.

By Diya Ladher

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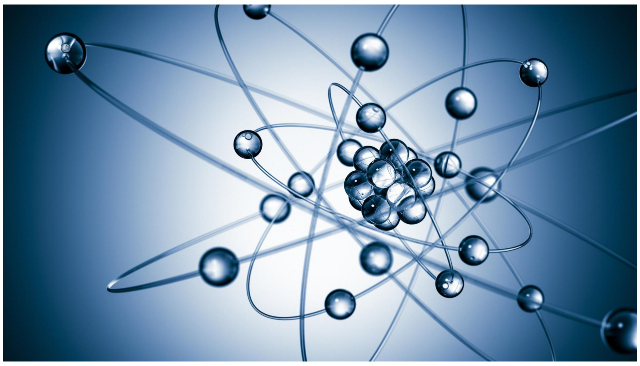

Neutrinoless Double Beta Decay: A Gateway to New Physics Beyond the Standard Model

For decades, the Standard Model of particle physics (SM) has served as a robust theoretical framework, accurately predicting the behaviour of almost every subatomic particle. Its notable triumphs include foreseeing the existence of the Higgs Boson, top quark, and W/Z bosons before their experimental discovery. However, it is insufficient for predicting the overwhelming predominance of matter in the universe. While the SM can generate a slight asymmetry, it fails to account for the observed baryon asymmetry of the universe by many orders of magnitude. This indicates that new physics beyond the SM is required to explain the prevalence of matter.

Despite the SM treating leptons and antileptons as distinct entities by assigning them opposite quantum numbers, the unique nature of the neutrino offers a potential solution to the question of baryonic asymmetry. If the neutrino is its own antiparticle–a Majorana fermion–it would allow processes where lepton number is not conserved. This lepton number violation provides a mechanism for leptogenesis, forming a pathway to explaining the universe's matter-antimatter asymmetry. A frequently proposed theoretical process that would prove a Majorana nature of the neutrino is neutrinoless double beta decay.

When beta decay was first discovered in the late 19th century, an issue appeared involving the process' association with the conservation of energy. Beta particles emitted often have a range of energies, yet it was frequently found to be less than what scientists predicted. Thus, during 1930, Swiss physicist Wolfgang Pauli postulated the existence of the neutrino [1]. This particle was stated to be an electrically neutral, low mass particle that would be emitted along with the beta particle.

Later, in 1935, Maria Goeppert Mayer proposed the concept of double beta decay [2]. In this process, two neutrons simultaneously decay into protons with the emission of two electrons and two antineutrinos. Her calculation showed that while immensely rare, this decay was theoretically possible for specific nuclei where standard beta decay is prohibited. Following this, physicist Ettore Majorana introduced the concept of a particle being its own antiparticle [3]. This was later labelled as a Majorana particle.

Once Goeppert Mayer's and Majorana's theories were combined, neutrinoless double beta decay was hypothesised. Unlike the standard second-order weak process–a rare event where two separate radioactive decays happen simultaneously, producing two antineutrions–neutrinoless double beta decay occurs without any neutrino emission. In the case where a neutrino is a Majorana particle, it is possible that two neutrinos could annihilate each other without the presence of an antineutrino. If discovered, neutrinoless double beta decay could reveal the immense flaws of our current understanding of particle physics and the universe. Firstly, it would help determine the absolute scale of the neutrino mass spectrum, which physicists have attempted to solve since it was first discovered that neutrinos have mass [1]. Secondly, neutrinoless double beta decay would be the first evidence for any lepton number violation in nature, ultimately explaining the baryon asymmetry of the universe.

Many different global experiments are working to detect this phenomenon, such as the research at SNOLAB taking place in spherical acrylic vessels [4]. These vessels are filled with a liquid known as a scintillator, a substance that emits light when a charged particle, such as an electron, interacts with it. Once light is emitted, sensors called photomultiplier tubes (PMTs) capture the photons and convert them into electrical signals [4]. By utilising the photoelectric effect, the PMTs release electrons that trigger an internal amplification cascade, turning faint light into a measurable pulse sent to servers. If only two electrons are emitted, with an absence of neutrinos, they would be expected to carry the entirety of the decay's energy. The PMTs detect this by measuring the total intensity of the resulting light, allowing researchers to identify the specific energy signature that proves the existence of neutrinoless double beta decay.

The primary obstacle in detecting neutrinoless double beta decay is the utter rarity of the event, with predicted half-lives exceeding 10^26 years, trillions of times longer than the age of the universe [5]. To catch such an infrequent signal, experiments must achieve ultra-low background environments. Even trace amounts of natural radioactivity from surroundings such as laboratory walls, experimental hardware, or cosmic rays can mimic the signal of a decaying nucleus. This provides us the reason why SNOLAB and similar facilities are located deep underground, using kilometres of rock as a shield to filter out cosmic interference. Without this extreme isolation and the use of hyper-pure materials, neutrinoless double beta decay would be exceedingly difficult to detect.

Although neutrinoless double beta decay is a widely supported theoretical process that would prove the existence of Majorana particles, to this day it remains experimentally unobserved. Its eventual discovery would introduce a new physics beyond the Standard Model, possibly altering humanity's understanding of the universe indefinitely and providing the missing link in our comprehension of the nature of matter.

By Eve Williams

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The Effects of AI Usage in Healthcare

With the introduction of one of the first publicly available Large Language Model LLM, ChatGPT in November 2022, the way people searched and used the internet changed. ChatGPT quickly became a household name, reaching 100 million users in just two months, and has since reported more than 700 million users per week [1]. The uses of these models can range from writing an essay for homework, to answering maths questions, and even becoming a companion. Additionally, there is a rising trend, especially among young people, of using ChatGPT and other AI chatbots for medical advice.

One in 6 people under 30 in the US said they have used ChatGPT for medical advice, and nearly 80% of adults surveyed in 2023 said they would use ChatGPT to diagnose health symptoms [2]. For some, the benefits of using ChatGPT are seemingly obvious; a chatbot does not judge, it is available at all times of day, and it can draw from a database of millions of medical publications and papers. However, most people are unaware of the reality of using ChatGPT as a substitute for real medical advice.

The Psychology of Algorithmic Trust

ChatGPT is a quick, cheap and seemingly confidential resource, available to almost anyone in the world for free, at a time when many people globally cannot easily access affordable healthcare. One reason people may trust ChatGPT is that it is designed to produce helpful, polite and non-confrontational responses, which can make it feel reassuring [3]. Research on conversational AI also shows that systems can adapt to a user's tone and language to improve engagement. As a result of this, responses may align closely with a user's perceived perspective detected in their phrasing, which can reinforce their views and encourage continued interaction. If the user positively phrases a question by using words like 'is it true that…' or 'I think that', it will respond affirmatively, and the same is true for a negative question [4]. This means that it will affirm whatever the user thinks the issue is, regardless of whether this is actually the correct diagnosis.

In the case of a medical emergency, ChatGPT confirming someone's untrue beliefs could cause serious harm to a patient. In a case published in the Springer Nature journal, a man in his 60s with vision problems following a cardiac procedure had delayed seeking urgent medical care because he had spoken to a chatbot. He claimed that he did not understand what his doctor had told him, so he spoke to ChatGPT, which assured him his symptoms were benign and unremarkable, mirroring the man's own views. However, his symptoms were severe, and he was later diagnosed with a transient ischemic attack, or a 'mini stroke', a potentially serious medical emergency [5].

The Impact on Health Anxiety and The 'Nocebo' Effect

Research has repeatedly shown that internet use for health information has grown substantially since the early 2000s, with the development and spread of internet usage across the globe [6]. There has been extensive coverage of the 'doctor Google' phenomenon, and a large discourse around the way people diagnose themselves, using online resources such as WebMD's symptom tracker [7]. Health information-seeking behaviour (HISB) has become increasingly common, intensifying the risk of cyberchondria, a phenomenon where excessive repetitive online symptom searches can increase anxiety and cause distress, often leading to self diagnosis of severe illness. Numerous studies have evaluated its effects on mental health and diagnostic outcomes, highlighting its significance. Research has also examined how HISB varies across different socioeconomic backgrounds and factors.

There is a documented correlation between people looking up symptoms of a disease and experiencing the symptoms themselves [8]. They believe they have a condition, find the symptoms of it, and then themselves experience the symptoms more severely. In studies, it has been found that people who are given a placebo sugar pill and told it would give them symptoms such as headaches and nausea reported that they experienced headaches and nausea, despite the pill containing no active ingredients. This is known as the 'nocebo' effect [9]. This effect has been amplified with the rise of LLMs as people could develop health anxiety believing that they are unwell, due to incorrect diagnoses.

Systematic Bias and Demographic Disparities

In medicine, there is an unconscious bias often referred to as the 'gender pain gap', in which women's pain is dismissed as being over exaggerated or not real. This leads to the underdiagnosis and undertreatment of pain in women [10]. Research shows that ChatGPT has inherited this implicit gender bias, meaning that it often gives biased information to women [11]. This bias is a result of the way LLMs are trained. ChatGPT works by analysing existing data, using data that is itself biased due to systematic prejudices, including the historical exclusion of women from medical trials until the 1990s [12], [13].

Data Privacy and Ethical Compliance

For some people, talking to a doctor can be very intimidating, especially when discussing intimate or embarrassing topics. People may feel more comfortable talking to a screen rather than a real person. However, ChatGPT may seem confidential, but when users input health data, it is transmitted to external servers and may be used to improve the system [14].

Furthermore, ChatGPT can hallucinate or fabricate medical information when unable to generate an accurate response [15], [16]. Research has found that ChatGPT incorrectly diagnosed more than 8 in 10 paediatric case studies [17], raising serious concerns about the safety and reliability of the information ChatGPT generates. The increasing use of ChatGPT by doctors as well as patients, to process patient information also raises legal and ethical issues, particularly regarding GDPR and HIPAA compliance [14]. The sharing of patient data with the ChatGPT database could be considered to be a breach of these rules, and could lead to legal action against doctors.

Conclusion

AI has become an integral part of modern life, and is used by the vast majority of the population in some way. If people remain unaware of the risks using these systems poses, they will keep using them, potentially putting themselves and others at risk. Safer integration strategies are needed, such as secure GP messaging systems that preserve accessibility while avoiding hallucinations and misinformation [18].

By Hannah Warren

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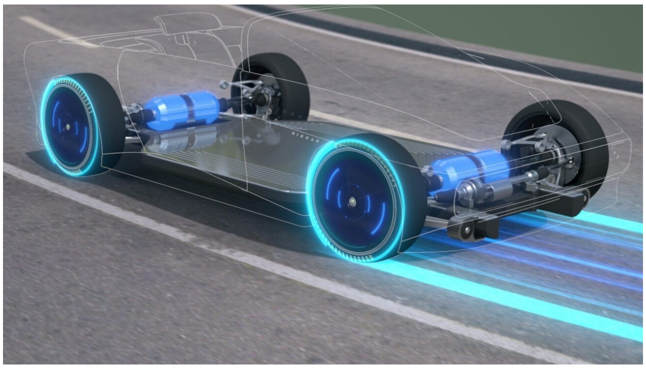

Regenerative Braking: From Brakes to Batteries

Every day, millions of vehicles travel on roads across the globe, and every time one of them brakes, kinetic energy is lost as heat. Regenerative braking offers a solution by recovering this energy and converting it into electrical energy for reuse. In a world increasingly concerned about sustainability, this technology is a significant step towards greater energy efficiency.

Every moving object carries a certain amount of kinetic energy. This can be defined by the formula: $E = (0.5)mv^2$, where m is the mass of the body and v is its velocity. This shows that an object moving at high speed possesses a great amount of kinetic energy. During braking, this energy needs to be dissipated. According to the law of conservation of energy, energy can neither be created nor destroyed; it can only be converted from one form to another.

In traditional vehicles, when the brakes are applied, the brake pads press against the discs, causing the vehicle's kinetic energy to convert into heat through friction. This heat is released into the airstream, and the energy is irreversibly lost [1]. The amount of heat released depends upon the duration, intensity and frequency of braking [1]. In urban traffic, the estimated amount of energy lost due to friction braking is 30-50% of the total traction energy consumed in an EV [2]. For example, a Formula One car of mass 798 kg [3], moving at 300 km h^{-1} (=83 m s^{-1}) has $KE = (0.5)(798)(83)^2 = 2{,}748{,}711$ J. This can also be expressed as 2.75 MJ.

Regenerative braking can help address the problem of energy waste. During braking, the electric motor acts in generator mode, reversing the direction of the torque and energy flow [4]. This reversal is caused by the vehicle's momentum. Every moving vehicle possesses momentum—the property of a moving body that allows a car to keep going forward when it is already at speed. In normal driving, the battery sends electricity to the motor, which spins the wheels and causes the car to move. During braking, the electric supply to the motor is stopped. However, the car still possesses momentum and continues moving forward. This momentum causes the wheels to spin the motor rather than the motor spinning the wheels. As a result, the energy flow is reversed and electrical energy is sent back to the battery rather than being drawn from it. The motor, therefore, acts as a generator, converting mechanical kinetic energy into electrical energy.In the majority of electric vehicles, this newly generated electrical energy is stored in a battery pack [5]. The amount of energy entering the battery pack is regulated by an electronic system known as the Battery Management System (BMS) [4], a device dedicated to the oversight of a battery pack, monitoring and regulating the charging process. The amount of energy recovered is influenced by many factors such as ambient temperature, charging rate and state of charge (SOC) [4]. The state of charge refers to the current charge level of the battery. The amount of regenerative energy that can be accepted is inversely proportional to the SOC, therefore the higher the charge level, the less energy can be recovered. Studies suggest that regenerative braking systems are capable of recovering 25-40% of the braking energy [2]. This recovered energy can extend a vehicle's range by 10% [6].

Although often regarded as modern technology, regenerative braking was first implemented in the late 1800s, when a French engineer, Louis Krieger, attached motors to the front wheels of his horse-drawn carriage [7]. These motors acted as brakes whilst also recovering energy. In the early 1900s, the Raworth system was introduced to trams in England, saving energy and allowing operators to control the trams better on slopes [7]. This proved highly beneficial; however in 1911, there was a fatal accident which led to the prohibition of regenerative braking [7]. Although reintroduced in the 1930s, there was limited implementation. At the time, petrol cars and the fossil fuel industry were dominant, leaving little incentive to prioritise energy-saving technology [7]. Today, the growing concerns over sustainability and energy efficiency have led to the revival of regenerative braking technology.

Regenerative braking is found across a wide range of applications, from road vehicles to surprising industrial uses. In hybrid vehicles such as the Toyota Prius, regenerative braking is used alongside a conventional engine, recovering energy during every braking event, without being plugged in [8]. Electric vehicles such as the Tesla take this even further. When the car is not accelerating it automatically recovers energy without requiring the brake pedal. This is known as one pedal driving, and it is based on regenerative braking [9].

Regenerative braking systems are also implemented in trains. In urban network systems, regenerative braking returns energy to the power distribution network, which can be used to power other trains or other electrical demands, such as station lighting. This allows energy savings of 8-17% in standard commuter networks and about 30% in dense suburban networks [10]. Beyond transportation, regenerative braking is also implemented in elevators. The descending cars act as generators to recover energy that would have otherwise been wasted. Studies suggest energy savings of 20-40% [11]. In each case, the concept remains the same, capturing and reusing energy that would have otherwise been lost as heat.

Formula One represents one of the most extreme applications of regenerative braking systems. Formula One uses the Motor Generator Unit-Kinetic (MGU-K). This is the regenerative braking system of the Formula One hybrid power unit [3]. The recovered energy is stored in a dedicated onboard battery, known as the Energy Store. During acceleration, this energy can be deployed to provide extra power [3]. This was originally implemented along with the Motor Generator Unit - Heat (MGU-H) in 2014, where it provided up to 120 kW (160.9 hp) [3]. Under the 2026 regulations, the MGU-H has been removed, leaving the energy recovery solely on MGU-K, which gives almost 3 times the power of 350 kW (469.3 hp) [12].

The energy recovery system (ERS) can recharge the battery with up to 9MJ per lap. This harvested energy can be deployed by the drivers via the boost button on the steering wheel [12]. This increase in the electrical power means the hybrid element contributes to almost 50% of the total power, making energy management a critical strategic element for both the drivers and the engineers [12]. Unlike conventional electric vehicles, Formula One systems must recover and redeploy energy within fractions of a second [12].

Despite its numerous benefits, regenerative braking still faces several challenges. Firstly, the significant hardware demands as well as their computational complexity increase the overall cost of the vehicle [4]. This hinders the widespread adoption of regenerative braking systems in mass-produced vehicles, particularly for budget-conscious customers. Secondly, regenerative braking alone is insufficient to perform emergency stops. This requires every vehicle to have a conventional braking system, alongside the regenerative braking system, increasing component complexity for the manufacturers [13]. Thirdly, the repeated charging and discharging of the battery occurring every time the brakes are pressed results in battery degradation over time, which may necessitate more frequent battery maintenance or replacements [4]. Finally, regenerative braking works best at high speeds. At low speeds, such as in crawling traffic, the vehicle has insufficient momentum to generate electricity. This means much of the braking energy that could be recovered is lost as heat [4].

Despite these limitations, regenerative

braking still remains a prominent tool for sustainability. From the physics and origin to its real-world applications and challenges, this technology is now more relevant than ever. The scale of energy wasted through conventional braking is considerable.

Remarkably, a technology over a century old is now at the forefront of energy recovery. As regenerative braking becomes more widespread, its potential to reduce global energy consumption becomes increasingly significant.

By Kavya Balan

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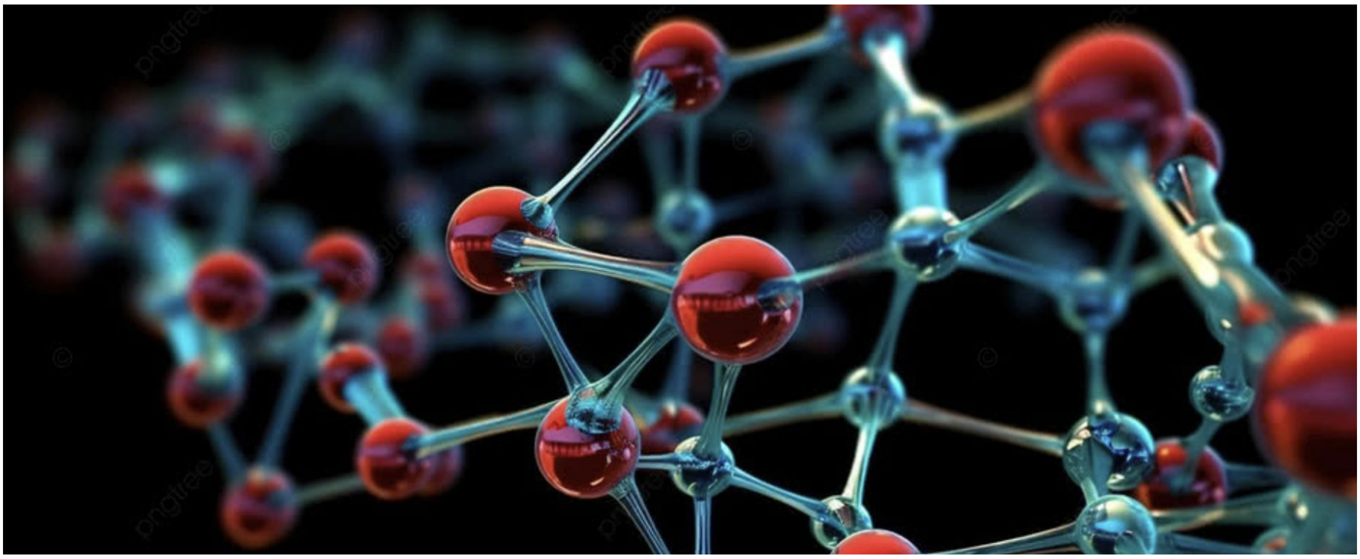

The Evolution of Chemical Bonds

Bonding is the process of electron interaction between atoms that allows them to form stable compounds [1]. There are several primary types of chemical bonds. Ionic bonds are formed when electrons are completely transferred from one atom to another [2]. This transfer creates charged ions—positively charged cations and negatively charged anions—which attract each other through electrostatic forces [2]. A common example is sodium chloride (NaCl) [1].

In contrast, covalent bonds are bonds in which atoms share pairs of electrons, typically between non-metal atoms [3]. There are two main types of covalent bonds: polar and nonpolar. In polar covalent bonds, electrons are shared unequally due to differences in electronegativity, resulting in partial charges on the atoms [3]. In nonpolar covalent bonds, electrons are shared equally, often occurring between identical atoms [3].

Lastly, metallic bonds are characterised by a "sea" of delocalised electrons that move freely within a lattice of positively charged metal cations [4]. This allows metals to conduct electricity and heat efficiently [4].

The understanding of chemical bonding has developed over time through the work of many scientists. In 1830, Michael Faraday introduced the terms "ion," "anion," and "cation" through his electrolysis experiments, which demonstrated that charged particles are involved in chemical processes [5]. However, the exact nature of these particles was not yet fully understood. In 1884, Svante Arrhenius proposed that certain substances, such as salts, dissociate into ions when dissolved in water, even without the presence of an electric current [6]. This idea helped explain the conductivity of electrolyte solutions [6].

A major advancement came in 1916, when Gilbert Newton Lewis proposed that atoms form bonds by sharing pairs of electrons [7]. This concept became known as the covalent bond, a term later introduced by Irving Langmuir in 1919 [7]. Around the same time, Walther Kossel suggested that ionic bonds result from the transfer of electrons between atoms, providing a clear explanation for the formation of ionic compounds [8]. In the 1920s, Linus Pauling applied principles of quantum mechanics to chemical bonding and introduced key concepts such as electronegativity and resonance, which are still used today [9].

Further progress was made in 1927, when Walter Heitler and Fritz London developed the first quantum mechanical model of chemical bonding [10]. Their work focused on the overlap of electron orbitals, particularly in simple molecules such as hydrogen, and marked the beginning of modern quantum chemistry [10]. These developments were built on earlier atomic models, including Hantaro Nagaoka's 1904 theory of a positively charged centre surrounded by orbiting electrons, similar to the structure of Saturn and its rings [11]. In addition, Ernest Rutherford's 1911 discovery showed that atoms contain a small, dense, positively charged nucleus surrounded by electrons, providing a more accurate picture of atomic structure [12].

Ionic compounds form regular lattice structures, in which ions are arranged in an ordered three-dimensional pattern [2]. The strong electrostatic attraction between oppositely charged ions holds the lattice together [2]. For a bond to be stable, the energy released during lattice formation must be greater than the energy required to remove electrons from atoms [1]. This balance of energy explains why ionic compounds are generally stable and have high melting and boiling points [1].

Another important concept in chemical bonding is the octet rule. Gilbert Newton Lewis observed that atoms tend to lose, gain, or share electrons in order to achieve a stable configuration of eight valence electrons [7]. This arrangement is similar to the electron configuration of noble gases, which are chemically stable [1]. However, there are exceptions to this rule. Hydrogen and helium, for example, only require two electrons to achieve stability because they have only one electron shell [1].

The position of an element in the periodic table determines the number of electrons in its outer shell [1]. Elements in the first main group have one valence electron, while those in the seventh main group have seven valence electrons [1]. This difference explains why elements from these groups often react with each other. For example, sodium, a metal in the first main group, has one electron in its outer shell. Chlorine, a non-metal in the seventh main group, has seven electrons in its outer shell and needs one more to achieve a full shell [1].

Electron shells are filled in a specific order. The first shell can hold up to two electrons, while the second shell can hold up to eight electrons and is considered full at that point [1]. The third shell can also hold up to eight electrons in many cases, although it can expand further in more complex atoms [3]. The number of electrons in the outer shell determines how an atom will react chemically [1].

When sodium and chlorine come into contact, sodium transfers its outer electron to chlorine [2]. As a result, sodium becomes a positively charged ion, while chlorine becomes a negatively charged ion [2]. These oppositely charged ions attract each other and form an ionic bond, creating sodium chloride [2]. Both atoms achieve a stable electron configuration through this process [1]. This reaction is highly exothermic and releases a large amount of heat and light, demonstrating the strong attraction between the ions [2].

In modern chemistry, our understanding of bonding has become more advanced. While early models focused on simple electron transfer or sharing, scientists now use computational quantum chemistry to study electron behaviour in detail [9]. Concepts such as electron density, hybrid orbitals, and molecular orbitals provide a more accurate description of how atoms interact [9]. These models allow scientists to predict the structure and properties of complex molecules and materials [9].

Despite these advancements, the basic principles of ionic, covalent, and metallic bonding remain fundamental to chemistry [1]. They provide a foundation for understanding how substances form, how they behave, and how they interact with each other [1]. By combining classical theories with modern computational methods, scientists continue to expand their knowledge of chemical bonding and its role in the natural world [9].

By Margaret May Mullan

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The Role of The Gut-Brain Axis in Neurodegeneration

The gut microbiota refers to over 100 trillion microorganisms that live within the gut, mostly concentrated in the bowel [1]. These microorganisms consist of several thousands of bacterial species, in addition to viruses, fungi, and parasites [2]. The gut microbiome plays a crucial role that affects almost all areas of the body; it is involved in the digestion, immune, nervous, and endocrine systems. Gut microbiota can link to the central nervous system (CNS) through the gut-brain axis and its effect on neurological conditions, such as Parkinson's disease.

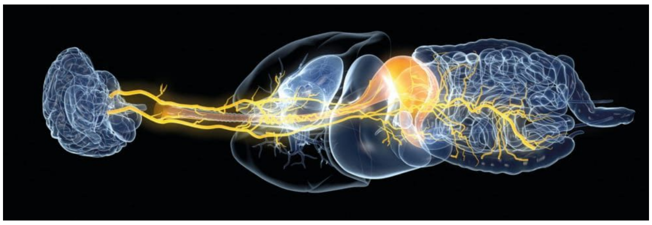


Fig 1: Vagus nerve

The gut-brain axis is the two way communication network that connects the intestinal microbiome with the central nervous system. The axis involves multiple layers of communication pathways, encompassing the immune, nervous, and circulatory systems [3]. The main nervous connection between the gut microbiota and the brain is the vagus nerve. This nerve contains 80% afferent fibres, and 20% efferent fibres, which face towards or away from the CNS respectively. Afferent fibres can sense gut bacteria in addition to their metabolites and transfer this information to the CNS. This is possible through special gut sensory epithelial cells, called 'neuropods' [4].

Short Chain Fatty Acids and Neuroinflammation

One of the key metabolic roles of the gut microbiome is the fermentation of dietary fibres into short chain fatty acids (SCFAs). These are both an energy source and signalling molecule that is critical to brain function [3]. SCFAs influence neuroinflammation through receptor-mediated mechanisms. One way they do this is the inhibition of the nuclear factor-κB (NF-κB) signalling pathway [3]. This pathway is critical for immune and stress response, B-cell development, and controlling inflammation [5]. SCFAs produce an anti-inflammatory response by binding to G-protein coupled receptors (e.g. GPR41/43) on the vagus nerve which triggers a signalling cascade that allows the gut microbiota to communicate directly with the CNS. By binding to these receptors, SCFAs inhibit the signalling pathway, preventing the production of pro-inflammatory molecules such as cytokines and chemokines [6].

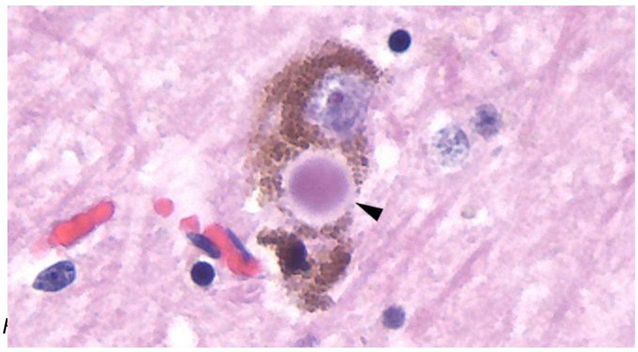
Neuroinflammation is the inflammation of tissue in the brain or spinal cord, induced by pathogens or physical damage. It is associated with almost all brain diseases, notably Parkinson's, Alzheimer's, and Huntington's diseases [7]. In the short term, just as with swelling in other body tissues, neuroinflammation is the result of immune response and plays a vital role in healing. However, if it is prolonged or 'chronic', more pro-inflammatory molecules are released that begin to damage healthy cells and tissues, including the blood brain barrier in the case of neuroinflammation [7].

The blood brain barrier is a layer of tightly packed endothelial cells that line the blood vessels in the brain and CNS. The cells have a lipid based outer membrane which naturally repels water soluble substances [8]. The blood brain barrier also includes cells called astrocytes and pericytes which help regulate blood flow and provide structural support. There is also an underlying layer of proteins that acts as an additional filter. This barrier is designed to prevent most substances from being able to enter the brain, bar a few small or lipid soluble molecules such as oxygen, carbon dioxide, caffeine and alcohol. It is 50-100 times tighter than the walls of blood vessels in other parts of the body [8].

If it is damaged, pathogens and immune cells are able to cross into the brain, causing further chronic inflammation and damage to neurones that can cause or worsen neurodegenerative conditions. For example, neuroinflammation can damage dopamine producing neurons which accelerates Parkinson's disease progression.

Overall, without a balanced and healthy gut microbiome, bacteria which ferment dietary fibre may be absent or reduced, causing the production of SCFAs to decrease. This would lead to increased neuroinflammation and potentially cause or accelerate neurodegeneration.

Body-First Parkinson's Theory



Parkinson's disease is a progressive neurological condition of the CNS that affects movement and cognition; notable physical presentations include tremors, slower movement, and muscle stiffness. These symptoms are caused by a lack of dopamine in the brain which arises when neurons in the substantia nigra area of the brain, responsible for producing dopamine, become damaged or die. Dopamine is a neurotransmitter that enables smooth coordinated muscle movement [9], [10]. Parkinson's can be caused or accelerated by the misfolding of a protein called alpha-synuclein which forms clumps called Lewy bodies. The accumulation of Lewy bodies in the brain stimulates the release of proinflammatory molecules by microglia cells which results in neuroinflammation [10].

The body-first theory indicates that misfolded alpha-synuclein might originate in the gut and spread to the brain and other parts of the body via the vagus nerve. Evidence for this claim is that toxic Lewy body clumps have been observed in the gut of some people up to 20 years before a Parkinson's diagnosis. Additionally, alpha-synuclein has been found in the vagus nerve, indicating its suitability as a transport link. Moreover, cutting the vagus nerve, which was done in the 1970s and 80s to treat ulcers, was linked to a reduced risk of Parkinson's, though later studies did not note a significant correlation [9], [11]. Lewy bodies found in the gut are thought to cause digestive complications such as constipation, which is an early symptom of Parkinson's. These protein clumps may also be able to travel along the vagus nerve to the heart which is thought to affect blood pressure [9].

A study performed by Dr. Nathalie Van Den Berge from Aarhus University, Denmark, demonstrated the spread of both body-first and brain-first Parkinson's in rats. The study involved injecting alpha-synuclein into the brains of some rats and the small intestines of other rats which had been modified to mimic symptoms of Parkinson's. After 4 months they studied the rats to see how the alpha-synuclein had spread. The rats which had the protein injected into their intestine represented body-first Parkinson's, and they experienced damage to neurons on both sides of the brain, in addition to the loss of nerve cells in the heart and gut. This indicates that alpha-synuclein travelled along the vagus nerve from the gut to the heart and brain, causing neuroinflammation and later neuron death.

The rats which had the protein injected into their brain represented brain-first Parkinson's, another theory which suggests that the disease originates in the brain and later spreads to other parts of the body.

When these rats were studied, they had nerve damage only in the half of the brain where the alpha-synuclein was originally injected; there was also no damage in other parts of the body. This may explain why some people with Parkinson's only experience tremors in one half of their body: they have brain-first Parkinson's, where Lewy bodies only affect one hemisphere of the brain [9]. It also shows the potential progression of alpha-synuclein from the gut to the brain, and the importance of the gut microbiome in the management of Parkinson's.

Dr. Sampson from Emory University School of Medicine, Atlanta, USA, identified individual microorganisms that appeared to be imbalanced in the gut microbiome of many people with Parkinson's. Upon testing these microorganisms on mice, some caused constipation, an early symptom of Parkinson's, while others were able to increase the clumping of alpha-synuclein. From this he and his team concluded that gut microbiome dysbiosis triggers the spread of alpha-synuclein. Though this research is still new, there is a definite link between an unbalanced gut microbiome and the cause or worsening of certain neurodegenerative conditions, such as Parkinson's [9].

Microbiota-Based Treatments

A new treatment that is in testing stages for people with Parkinson's is fecal microbiota transplant. Transferring stool from a healthy individual to the intestinal tract of someone suffering microbial dysbiosis, can restore a healthy balance of bacteria in their gut microbiome. This may reduce some of the symptoms of Parkinson's, like constipation, and reduce the formation of Lewy bodies which will lessen neurone damage from chronic inflammation.

A placebo controlled study published in NIH, used this treatment on people with Parkinson's and had promising results. The patients involved in the study tolerated the transplant well, with minimal significant side effects and there was reported improvement in motor symptoms and microbiota diversity increased over 12 weeks of treatment via capsules [12]. This form of treatment is still being developed but the study and others are optimistic about its feasibility [12], [13].

Conclusion

Overall, the disruption of the gut microbiome may actively contribute to Parkinson's disease through the gut-brain axis. By reducing beneficial SCFA production, promoting chronic neuroinflammation, and potentially facilitating the spread of misfolded alpha-synuclein proteins via the vagus nerve, dysbiosis may accelerate dopaminergic, and more general, neurone loss. Evidence from body-first Parkinson's studies and emerging fecal microbiota transplant trials further highlights the gut microbiome as a driver of neurodegeneration but also a potential target for therapeutic intervention.

By Maya Shah

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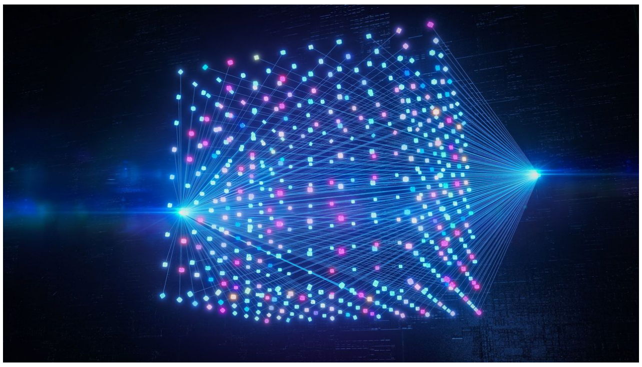

Beyond the Black Box: How AI is Decoding Chaos

On December 17th 2025, scientists at Duke University's Pratt School of Engineering created an AI model that solves the problems of black-box machine learning. Through their model of weather predictions, the study of Chaos has been revolutionised, allowing for human and artificial intelligence to work alongside each other.

A black-box system is one where there is strictly a user input and machine output; the steps taken to reach this output are hidden from the user. Due to the difficulty of showing how AI 'thinks', most AI models are black-box. Although they provide solutions quicker than white-box systems, black-box systems produce more errors. This is because the user relies on the algorithm to take logical steps to reach its outcome. If any mistakes occur in a black box, it would be difficult to identify where it happened, but even more complicated to teach it that its conclusion is wrong [1].

However, in detecting patterns and anomalies in a given set of data, white-box models have not been preferred. In order to give the user a breakdown of its processing, this system must create and explain the equations that it will use to produce results. Therefore, the model is learning and interpreting data simultaneously because it views all the values and creates its own set of rules for them. Hence, producing evidence for this abstract method would not be practical.

On the other hand, black-box models take slightly different steps for the same procedure. After the user inputs data, an algorithm will identify patterns in it. Then, logical rules are created that link most of the points, so the data can be interpolated. Importantly, the factors that were considered in giving this interpolated answer will not be shown to the user, usually due to too many being involved. Information for these factors is obtained from previous research in the AI's database. A common example of a black-box AI model is ChatGPT or Google Gemini.

In the opinion of Cynthia Rudin, a professor at Duke University, we should "stop explaining black box machine learning models for high stakes decisions", showing how she believes that the use of black-boxes in society should decrease [2]. This is especially relevant in medical diagnoses and criminal justice. Rather, more white-box models should be created and used so we can understand how a conclusion is reached. This allows for the decision to be explored, understood and challenged, which is fundamental to careers that are centred around people's futures and lives.

Contrastingly, some may argue that it inhibits artificial intelligence from reaching its full potential. By making the systems expand on the logic of every decision, it would slow down their response time and therefore their efficiency. It would also be difficult and time-consuming for humans to create such models, as this sector is not researched as much as black boxes due to the public preferring fast responses over deeply analysed ones.

To counter this, the long-term effects of introducing these models would surpass its short term ones. There would be a better understanding of the mistakes made by AI. This could deter the use of AI in professional, academic or high-risk settings. It could dispute the cultural issue of humans being "domesticated" by AI models, as the Professor of Computer Science at the University of Swansea describes. Therefore, most of the ethical issues surrounding AI can be resolved through increased use of interpretable models over black-box ones.

A distinct feature of black-box architecture is its reliance on prediction, whereas white-boxes have set mathematical rules in place. The quintessential example of a white-box system is a linear regression model that creates a linear equation from data points. The model would output the equation with its gradient and y-intercept to show how the points link together. However, this can be seen as a drawback, as white boxes rely on rigid rules to draw conclusions. So, in chaotic or complex data sets, it will not be able to interpret them accurately. This is where black box models would be favourable.

Chaos Theory refers to the mathematical study of unpredictable courses or events [3]. An example of where Chaos Theory is crucial is in weather predictions. Due to its random changes, weather can never be predicted to a 100% degree of accuracy. Factors such as wind, temperature, and humidity prevent us from achieving full efficiency in weather forecasts. Mathematician Edward Lorenz created the Lorenz-96 climate model to show a simplified version of the Earth's atmosphere. This model contained over 40 linear and non-linear equations and numerous variables, showing how Chaos is difficult to work with. Furthermore, his renowned model is an example of deterministic Chaos. This is when a slight change in the initial values leads to a great difference in the results, often due to exponential elements. Subsequently, Lorenz became the founder of Chaos Theory, which scientists nowadays continue to analyse.

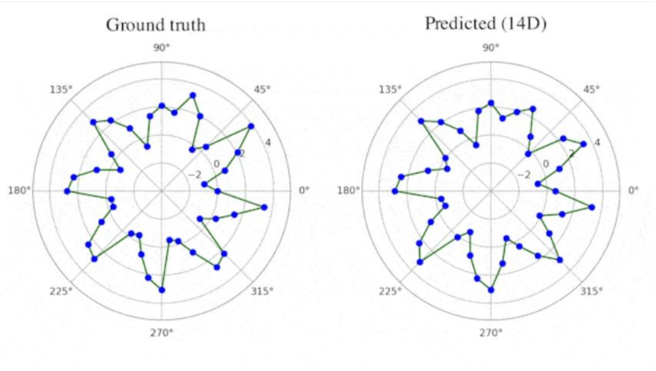

Figure 1

Duke University created an AI model that builds on the Lorenz-96 one by using AI to improve the accuracy of weather predictions as shown in figure 1. Moreover, it gives scientists the exact linear equations it derived to create the model, much like a white-boxes [4]. It builds on Lorenz's model as it can create hundreds of non-linear inputs, rather than just 40. Another impressive feature is that it predicts even the change of temperature fluctuations over time, showing how it finds new patterns for factors affecting the Lorenz model [5].

These new levels of accuracy were achieved by using the Koopman Operator Theory. Before, linearisation of data points would happen locally, where the computer would focus on a small portion of the data. Now, coordinates are embedded into a multi-dimensional space, allowing us to change the perspective from which the coordinates are seen. Consequently, a common equation can be found which lines up all the points from a different viewpoint. As an analogy, we can see the previous method as looking at a winding road from the point of view of the car. This angle would conceal some parts of the road, making it look confusing and incoherent. Koopman's method is like looking at the same road from a bird's-eye perspective to see how it follows a clear path. After implementing the Koopman Operator Theory, the specific equations in this "route" can be calculated. The university's model uses AI to do this as it is quicker for humans to check the equation rather than creating it.

Importantly, these derived equations can be further researched to uncover mathematical principles in weather predictability. It is here that this model can be very beneficial because it can be used to find new correlations in other fields. A more precise interpolating architecture means relationships between variables can be pioneered, and the implications of this would be immeasurable; better predictability in mathematical theories means the field of engineering, architecture, and science will be revolutionised.

Some notable socio-economic impacts could be better management of a city's power grid. Rather than risking an element of human error, this model could predict future power surges and blackouts more precisely ahead of time. This way, both the city and citizens would save money and resources. Crucially, if the machine were to make a wrong prediction, the equations that were used could be analysed by specialists and altered so it would not make that mistake again. Therefore, developing white-box AI proves to be valuable because it offers the chance of correction that black boxes struggle to accept.

Although the increased use of AI would mean fewer job opportunities, human scientists will still be needed to ensure the equations derived are appropriate and work as intended. Nevertheless, this profession would require more education, creating a more competitive field. On one hand, this increases the education rates in a country, but on the other hand, current employees in technology may find it difficult to qualify for future jobs. Additionally, in capitalist societies, this new opportunity to use machines rather than paying wages is beneficial to companies. This has the potential to create a new "boom" in international trade similar to that of the Industrial Revolution, but through digitalisation instead. Rather than coal being the raw material for producing products, machine learning will be the new fuel of industry.

In conclusion, this new branch of AI has transformed weather prediction and paved the way for white-box models to become the new norm in machine learning. This is significant as it allows for AI to be challenged, studied and developed for humans to be able to incorporate it into their lives in a more beneficial way rather than trusting its logic blindly. A surge in the integration of AI can also be expected due to Duke University's discovery, becoming the catalyst in machine learning innovations. While the societal advantages can be endless, from power grid optimisation to biological disease predictions, it poses a risk to the employment of tech staff and data analysts. Regardless, the life-saving benefits far outweigh the temporary disruptions to the labour market.

By Sarah Basheir

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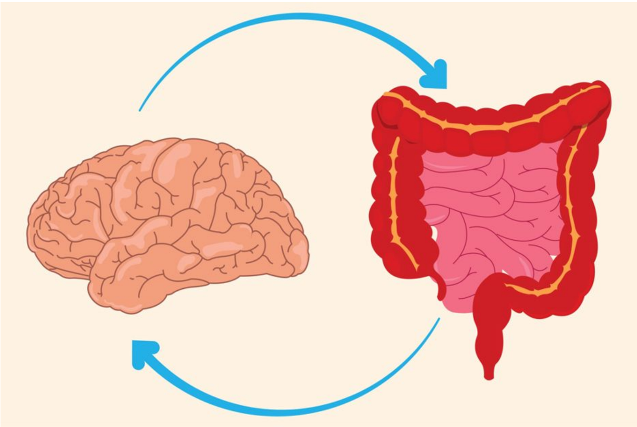
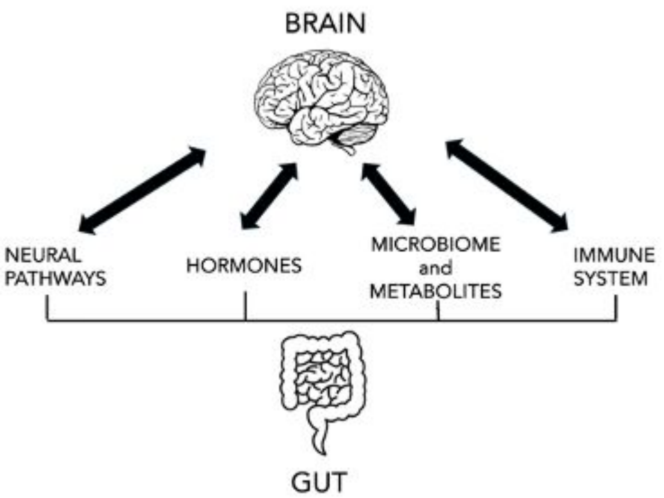


The Gut-Brain Axis: How The Gut Microbiome Affects Decision Making

For centuries, the brain has been perceived to be the “control center” of the body and the origin of thoughts, emotions, and decisions [1]. However, modern biology and its breakthroughs are challenging that assumption. Hidden within the human digestive tract is the gut microbiome, a vast system of microorganisms. Recent research suggests that this section of the body may play a significant role in how humans think, feel, and behave.

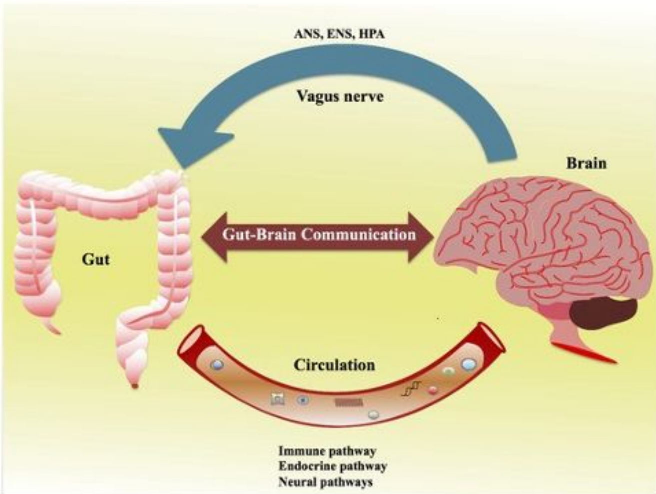
The Bidirectional Axis: A Complex System of Communication



The human gut microbiome is a diverse ecosystem that is composed of bacteria, fungi, and archaea. This ecosystem plays a vital role in the digestion of food. In addition to just digestion, recent research has shown to be consistent with the ancient Greek postulate that the gut is connected to the brain in both directions, indicating that the brain also influences gut function.

Gut functions are affected by the brain primarily through the hypothalamic-pituitary-adrenal (HPA) axis and the Autonomic Nervous System (ANS) [2]. Sympathetic and parasympathetic neural inputs regulate intestinal function and are likely responsible for the observed emotion-associated regional variations in gastrointestinal motor, secretory, and potentially immune activity [3]. In addition to neural modulation, sensory information in the gut is encoded through multiple pathways, including primary afferent neurons, immune cells, and enteroendocrine cells.

For example, under stress, the brain produces norepinephrine, a “fight-or-flight” hormone. This hormone promotes the proliferation of gut pathogens, which can influence gastrointestinal physiology by altering motility, secretion, and immune activity [4]. Additionally, the CNS sends direct signals to the gut to alter its physiology. This impacts gut epithelium, the cells lining the inner surface of small and large intestines, and influences the immune system activation. This happens either by impacting the immune cells’ response to the microbiome or by changing the microbiome’s interaction with the cells [5].



Additionally, the gut also affects the brain’s function. Not only does it maintain gut homeostasis, but is likely to have multiple effects on affect, motivation and cognitive functions. This is because the gut microbiomes actively participate in several neurodevelopmental processes, including neurogenesis and myelination. Cognition and brain functions are significantly affected by these processes as they depend on the nutrients and dietary molecules from the gut, especially during infant development [6]. In all, the ENS, ANS, and HPA work together to communicate with each other. As a result, the gut and its communications to the brain serve as a catalyst to the development that is necessary for humans

The Effects of The Gut-Brain Axis

The Gut-Brain Axis has had a long-lasting effect on the scientific and medical community. It has opened many doors for treatment and care for millions. Currently, there are many neurological diseases and conditions that are directly affected by the discovery of the GB axis [7].

Autism Spectrum Disorder (ASD) is a group of disorders particularly relevant when examining the role of the Gut-Brain Axis. ASD is a group of neurological disorders that affect how people interact socially and in communication. They lead to certain patterns of behavior, interests, and activities [8]. Recent research shows that these disorders are associated with changes in the gut microbiome. Since ASD are neurological conditions, the GB Axis links the gut and its microbiome to these disorders. Patients with ASD are often also accompanied with conditions such as gut dysbiosis, which is the imbalance of microorganisms in the body [9]. The treatment of these gut symptoms in ASD patients with Microbiota Transfer Therapy (MTT), which transfers healthy bacteria from a healthy individual to a patient, has been shown to improve GI symptoms, ASD symptoms, and the microbiome for at least 8 weeks after [10]. These findings highlight the potential of the Gut-Brain Axis as a target for therapeutic strategies.

Parkinson's disease (PD) is a prominent neurodegenerative disease that affects approximately 10 million people worldwide [11]. PD is characterized by the progressive loss of nerve cells in the part of the brain called substantia nigra, which plays a part in controlling the body’s movement and chemical signaling in the brain [12]. Nerve cells produce dopamine, which acts as a “messenger” between the brain and the nervous system to coordinate movement. When nerve cells in the substantia nigra are gone, dopamine is no longer produced and movement is lost or slowed [13]. Parkinson’s is characterized by alpha-synucleinopathy (α-syn), or misfolded proteins. Specifically, if the α-syn starts in the ENS, due to the G-B axis, it may travel to and from the CNS [14]. Additionally, research shows that changes in gut microbiota may contribute to the initiation and spread of α-syn [15].

Additionally, Robert Friedland, a distinguished cognitive neurologist from the University of Louisville, revealed that bacterial proteins may elicit cross-seeded misfolding, inflammation and oxidative stress, and cellular toxicity. He proposed that this initiates diseases such as PD and Alzheimer's [16], holding significant potential for the future of these diseases and their treatment.

Limitations

The influence of the Gut-Brain on neurodegenerative diseases is immense. However, it also has a significant effect on the cognitive ability of the brain. This is because of the functions of the gut microbiota. The gut microbiota can either produce neurotransmitters, affect current neurotransmitters through dietary metabolism, or do both in conjunction. This happens because as the microbiota digest components, they provide energy to the host so neurotransmitters can be produced [17]. Due to the crucial role neurotransmitters play in cognitive ability, this can lead to negative effects, especially with glutamatergic neurotransmission, which contributes to learning and memory formation [18], [19].

Conclusion

Overall, this research has shown that the Gut-Brain Axis is an incredibly influential bidirectional communication line that aids in the function of our body. The study highlights the importance of maintaining both gut and brain health. For example, taking care of the gut microbiome is especially important if improving cognitive function is a goal. One key significance in these findings is the Mediterranean diet. The Mediterranean diet has shown to be beneficial to the gut microbiome and conversely the cognitive ability of the one consuming it. Additionally, it can prevent cognitive decline [20].

Additionally, this has allowed for recent expansion of opportunities for therapeutic procedures and interventions for gastrointestinal and neurocognitive disorders and conditions. It also serves as a warning to humans to take care of both the gut and brain. This can be done by eating more probiotics and foods that help the gut function, as well as giving the brain a break when it is needed. Ultimately, it also shows us these findings echo ideas proposed as early as ancient Greek medicine.

By Shawmikh Shah

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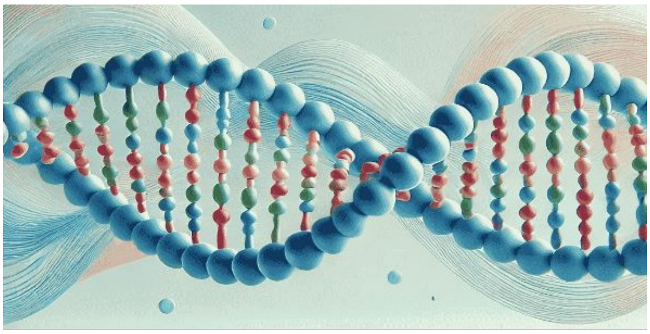

The Desi Alternative to CRISPR

The ability to precisely edit DNA has transformed modern biology, redefining how scientists understand and manipulate the genetic basis of life. As new gene-editing technologies emerge, older and more complex methods become increasingly relegated to specialized applications. The current widely used gene-editing technology is the CRISPR-Cas9/Cas12, which utilizes guide RNA (gRNA) and associated nucleases to introduce targeted modifications at specific genomic positions [1]. Prior to CRISPR, genome editing relied on technologies such as the zinc-finger nucleases (ZFNs) and transcription activator-like effector nucleases (TALENs). ZFNs were among the first programmable nucleases, followed by the more precise TALENs. Then, CRISPR revolutionized the field due to its relative simplicity and efficiency, with recent developments suggesting a new system that may compete with CRISPR-based technologies [1].

Overview of Transposon-associated Protein B

The new genome-editing system Transposon-associated Protein B (TnpB), derived from transposon-associated proteins, represents a significant development in genome editing, including emerging research programs in India. This new tool developed by the Indian Council of Agricultural Research (ICAR) is among the smallest RNA-guided nucleases to date capable of targeted genome editing in eukaryotic cells through the use of the TnpB and transposons [2]. This system may offer advantages over traditional CRISPR-Cas systems in specific applications due to its small size facilitating easier delivery into cells [1].

Transposons and Transposon-associated Protein B

Transposons, often referred to as the 'jumping gene', are chromosomal DNA segments that have the ability to undergo transposition. These elements are capable of moving from one genomic location to another within a cell and often bringing with them associated proteins, with one such protein being TnpB [3].

TnpB, similar to CRISPR-associated nucleases such as Cas9, functions as an RNA-guided endonuclease that introduces site-specific double-stranded DNA breaks, cleaving DNA at specific target sequences. Once the DNA is cut, cellular repair mechanisms can be harnessed to introduce targeted genetic modifications [3]. TnpB proteins, encoded by IS200/IS605 transposons are considered evolutionary precursors of Cas12 nucleases used in CRISPR-associated nuclease (CAs) systems [4]. While both the TnpB and Cas systems are RNA-guided DNA endonucleases, they differ significantly in size, function, and target recognition requirements [5].

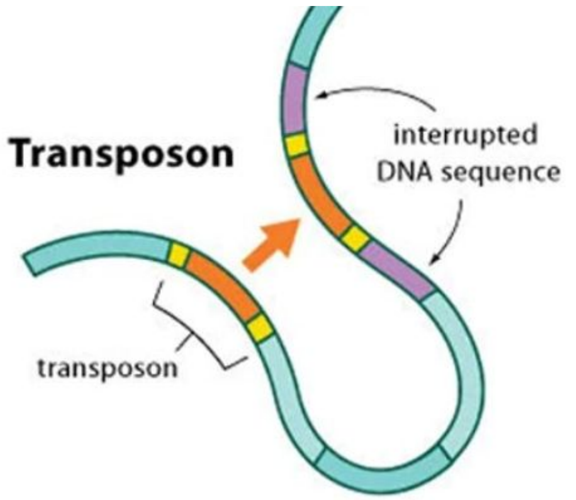

Fig 1. Transposon DNA Rearrangement [6].

Key Mechanism of TnpB

Beyond its origins, the functional mechanics of TnpB further distinguish it from pre-established genome-editing tools. The mechanism for TnpB is similar to that of

CRISPR-associated proteins like Cas9 and Cas12a, which revolutionized modern genome-editing. A chief feature of TnpB is that its proteins comprise 400–500 amino acids, which is nearly half the size of Cas9 and Cas12a, made up of 1,000–1,400 and 1,300 amino acids respectively [5]. The smaller protein facilitates more efficient delivery into plant cells and can be more easily packaged inside viral vectors, which allow the genetic material to be safely delivered into the cell's nucleus. This is where the cell's machinery translates the genetic code into TnpB protein, allowing it to bind to the ωRNA to form an active ribonucleoprotein (RNP) complex. The usage of TnpB potentially reduces reliance on complex tissue culture-based delivery methods. Due to this difference, TnpB may be especially useful for genetically modified organisms (GMOs) and in agricultural biotechnology as a whole [5].

Limitations of TnpB

There are a few limitations that come with TnpB’s compact size [4]. Many naturally occurring TnpB enzymes have low intrinsic gene-editing activity due to their function being facilitating DNA movement within bacterial genomes, not the highly-specific nuclease for eukaryotic genome engineering. The TnpB genome editing system’s targeting is limited by its requirement for a specific Transposon-Associated Motif (TAM), which unlike the NGG protospacer adjacent motif (PAM) used by Cas9, limits available genes that the system can target.

This causes TnpB to require intense optimization through significant protein engineering to TnpB’s protein and its guide RNA (ωRNA), to have higher nuclear localization, better targeting, and increased endonuclease activity. This may allow TnpB to reach Cas9’s level of efficacy, although it may increase experimental complexity [6]. This highlights a tradeoff in genomic editing, where increasingly compact sizes may come at the cost of flexibility and efficiency.

Implications on Biotechnology

TnpB has significant implications on the field of biotechnology, especially within emerging research ecosystems, by potentially reducing reliance on foreign licensing frameworks and opens the door to more affordable innovation in regards to the agricultural, medical therapeutics and industrial technology fields [5]. As the TnpB technology has been granted a 20-year patent by the Indian Patent Office and an international patent under the Patent Cooperation Treaty (PCT) to secure global rights and commercial protection. Tnp’s ability to change a single nucleotide in DNA without causing double-stranded breaks offers a safer mechanism for treating hereditary genetic defects, such as the ability to edit malfunctioning genes directly in patients' tissues in more sensitive areas like the liver or the brain.

In addition to that, due to TnpB’s compact size, it can be easily delivered into cells using AAV (adeno-associated virus) vectors. In contrast to the inconvenience of the delivery of large CRISPR-Cas systems due to AAV vectors having a limited carrying capacity of less than 4.7 kb [5]. This may help overcome major delivery limitations in both human and plant engineering, particularly for in vivo therapies and complex crop modifications. This system may be used to treat genetic disorders by enabling targeted genome modifications, such as insertions or deletions (indels).

TnpB may also enable advances in transgene-free plant editing, as it is able to use plant viral vectors to induce heritable edits without leaving foreign DNA in the organisms. This technology would create climate-resilient and pest-resistant varieties, contributing to higher yields and better nutrition. An example of this would be Engineered TnpB variants (eTnpB), which are modified versions of natural TnpB, designed to overcome the low efficiency and limited activity of natural TnpB when used as a genome-editing tool. eTnpB has surpassed other compact editors in a 90% editing efficiency in model plants such as N. benthamiana and successfully edited rice and pepper plants [7].

Conclusion

As biotechnology continues to advance and evolve, TnpB represents a promising step toward more compact and accessible gene-editing systems. However, its long-term impact will depend on further optimization with established tools such as CRISPR-Cas systems. In the end, the development of TnpB reflects a broader trend toward diversifying the available gene-editing technologies for more precise genetic engineering.

By Supasini Adhiphandhuamphai

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The Nature of Photosynthesizing Slugs

The same thing has been taught all around the world for decades: that animals acquire energy chemically while plants are the only organisms who photosynthesize. However, recent studies have disproven this theory, as researchers have found an order of animals that are able to harness energy from light. Sacoglossans are a category of sea slugs who gained fame for their ability to utilize chloroplasts from the algae they consume to create additional energy for their body to use.

The Requirements For Photosynthesis

The leaves of algae, like any other plant's, are made of plant cells. This means that inside those cells, there is a special organelle, called the chloroplast, which is responsible for transforming water and carbon-dioxide into oxygen and glucose, the latter of which is a molecule holding potential energy. With cellular respiration, the process of breaking glucose down using oxygen, ATP can be produced.

These chloroplasts are made up of many disks called thylakoids, which contain pigments, like chlorophyll, to absorb light. In order for light-dependent reactions to work, the clusters of pigments called the photosystems have to stay intact, otherwise no light will be absorbed, no electrons will gain momentum, and therefore later on no energy can be produced [1]. As photosystems are very susceptible to environmental stress, such as excess light or extreme temperatures, they are dependent on cellular repair components to make up for damages by replacing harmed photosystems with new ones. Most steps of this process take place inside the chloroplast, but for the synthesis of inevitable proteins, the cell's parts outside of the chloroplast are crucial [2], which is why these organelles should not function on their own, if taken out of their cell.

How Sacoglossans Keep Chloroplasts Alive

Chloroplasts in the slugs' bodies are referred to as kleptoplasts, as these organelles are not authentic but stolen, and were observed to have stayed unharmed for periods ranging from several weeks to years after consumption [3]. There are overall three consonant reasons as to why sacoglossans can preserve kleptoplasts, unlike other herbivores: non-photochemical quenching being triggered in the animal's body, a slower pace of electron transportation, and a mechanism replacing flavodiiron proteins, that are crucial for protecting photosystems after the binding of electrons.

Typically, when Photosystem II in thylakoids' membranes absorbs light, the electrons in chlorophyll gain energy to move on to an electron transport chain. These electrons are then replaced by electrons extracted from water molecules that are already in the thylakoid, which leaves oxygen and protons as the product of this exchange. In the meantime, the electron transport chain transports electrons to Photosystem I while the electrons pump protons from outside of the membrane into the thylakoid. This high concentration of protons is then passively diffused with the help of an enzyme called ATP Synthase, that produces ATP molecules from the flow of the protons.

Usually the protons are pumped into the thylakoid in the same pace as they leave, but when there are more protons flowing in, that additional energy is converted into heat, therefore protecting the photosystems from any harm. This process, called non-photochemical quenching (NPQ), works just as well inside the slugs. A lot of proteins can gather between the membranes inside the sacoglossans, which triggers high levels of NPQ, which ensures the safety of the photosystems [4].

Furthermore, the electron transport chains in the slugs' bodies, made up of intermediate molecules known as plastoquinones, are kept in a state that allows them to accept more electrons which ensures a slower transportation pace. This is essential as it prevents the over-accumulation of electrons that would otherwise lead to highly reactive and destructive molecules damaging the photosystems. So with the risk of harm being much lower, kleptoplasts are again guaranteed a longer life [4]. Sacoglossans have also developed an alternate way to deal with electrons after they had passed through the second pigment cluster, Photosystem I. In algae, flavodiiron proteins can bind electrons before they can cause any destruction when chloroplasts are turned into kleptoplasts [5].

Sea Slugs' Ability To Survive Off of Light

Sacoglossans have adapted to pick algae that already have stable photosystems, with flavodiiron proteins ensuring an even higher level of safety, while also having a tendency for a slower flow of electrons. Additionally, sea slugs can consume them whenever they would like. An experiment shows one slug who after consuming the alga, did not eat for 46 days, of which for only the first six days did Photosystem I stay active in the thylakoids' membranes [4]. So while kleptoplasts, for a limited amount of time, are able to function properly just as if they were in an alga's plant cell, the ATP generated by these organelles is a minimal contribution to the slug's body. Instead, the access to a fridge-like storage is what gives the advantage to these organisms when trying to stay alive without a food source nearby.

The Special Case of *Elysia Atroviridis*

The sacoglossan species *Elysia atroviridis*—commonly referred to as the Lettuce slug, is an exceptional instance amongst the photosynthesizing sea slugs. These creatures depend on energy acquired from kleptoplasts when trying to get rid of parasites, or when they get tangled up in seaweed. In these cases they are able to chop their own heads off and then regrow a completely new body in just a few weeks.

Autotomy, the ability of animals to voluntarily shed their body parts, has been observed amongst multiple species, including lizards, octopuses, crabs and lobsters, where these creatures defend themselves by letting go of their limbs or tails that have been grabbed, in order to not get caught by predators. However the case of the Lettuce slug has not been observed anywhere else throughout the animal kingdom. The exact process is still unknown but scientists suspect that multipotent cells, that have the capability of differentiating into specialized cell types, typically within a specific tissue or organ, play a role [6].

Conclusion

While there are still many unanswered questions, these small marine creatures have already shown many unique traits. Sea slugs may contribute to scientific research of recreating photosynthesis without the natural environment, while also giving insight on the most efficient tactics for regeneration.

By Zsófia Gyarmathy

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Thank You!

This concludes the eighth issue of the Penrose Magazine. Thank you so much for reading and we hope you enjoyed!

Finally, we would like to thank our team for all the work they put into editing, promoting, and formatting this issue.

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