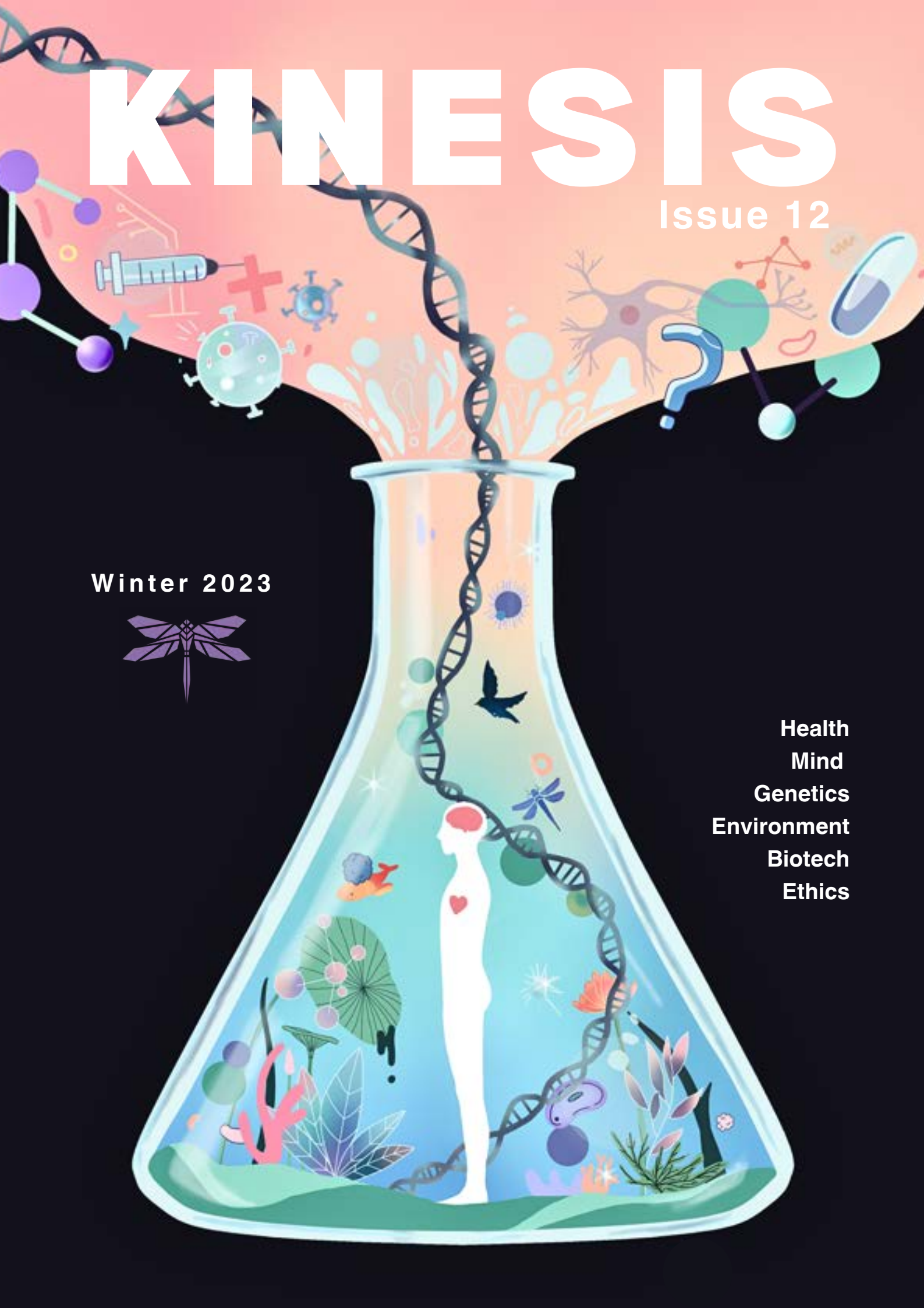
KINESIS

Issue 12



Winter 2023

Health
Mind
Genetics
Environment
Biotech
Ethics

A LETTER FROM THE EDITOR

I'm truly elated to introduce you to Kinesis Magazine's 12th Issue! An ode to the enduring significance of science communication, the vibrant pages of this print issue display the combined efforts of many talented authors, editors, and artists. It was such a joy to collaborate with this year's committee and, as always, it is entirely satisfying to see the successful outcome of our dedication.

Covering all facets of the circle of life, from genomics and nutrition to cell death and disease, this issue provides an astonishing overview of all that makes us human. Our essential humanity is contextualised by articles exploring the biology of the environment we see around us. Providing the necessary third dimension are articles about culture and psychology, completing our comprehensive overview of what it means to be alive in the modern day.

What better way to foster understanding and appreciation for the many wonders of our natural world than through the practice of science communication? This is not just another science magazine, but a vital brick in the bridge between two divided worlds: the pay-walled, complex world of research and that of the inquisitive public peering in from the outside. To our readers, it is the empowerment afforded by knowledge; to our contributors, it is the joy of expressing their passions.

A warm thank you to my fellow committee members and all of this issue's contributors! It was a pleasure to work with you.

Happy reading!

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Special Thanks to Yasmin Yong for the Cover Art

CONTENT

Health

Mind

Genetics

ENVIRONMENTS

Environment

Biotech & Ethics

The Fallen Angel

T Cell Senescence and Role in Inflammation

Harper Ling

Illustrated by Qiwen Liu

Why are older people more likely to suffer from chronic inflammation? Why is vaccine efficacy reduced in older people? People might attribute those age-related deteriorations to a simple reason: immunity declines as an individual ages.

But what does declined immunity mean?

Helper and cytotoxic (CD4+ and CD8+, respectively) T cells, both excellent guardians in adaptive immune systems, undergo senescence (the process of ageing).

Both activated by antigen-presenting ligands, CD4+ T cells are responsible for interacting with B cells to produce antibodies or secreting cytokines which generate signalling cascades on other cell types to clear the pathogens, while CD8+ T cells directly kill the cells by engulfing pathogens in a process called cytotoxicity. "Senescent" does not necessarily mean less "powerful" or "functional." Here, it refers to the final stage of T cell differentiation. Compared to less differentiated T cell stages such as central- and effector-memory T cells, several key functional differences of senescent T cells (TEMRA) are: reduced proliferative capacity, reduced specificity, and unexpectedly, greater cytotoxicity. TEMRA is less likely to increase its cell number in response to invading pathogens and less capable to distinguish "self" and "non-self," but kills more cells. Moreover, TEMRA tends to accumulate more in older individuals than in young people. Hence, immunologists have been driven to unravel phenotypic characteristics and functional roles of TEMRA in ageing.

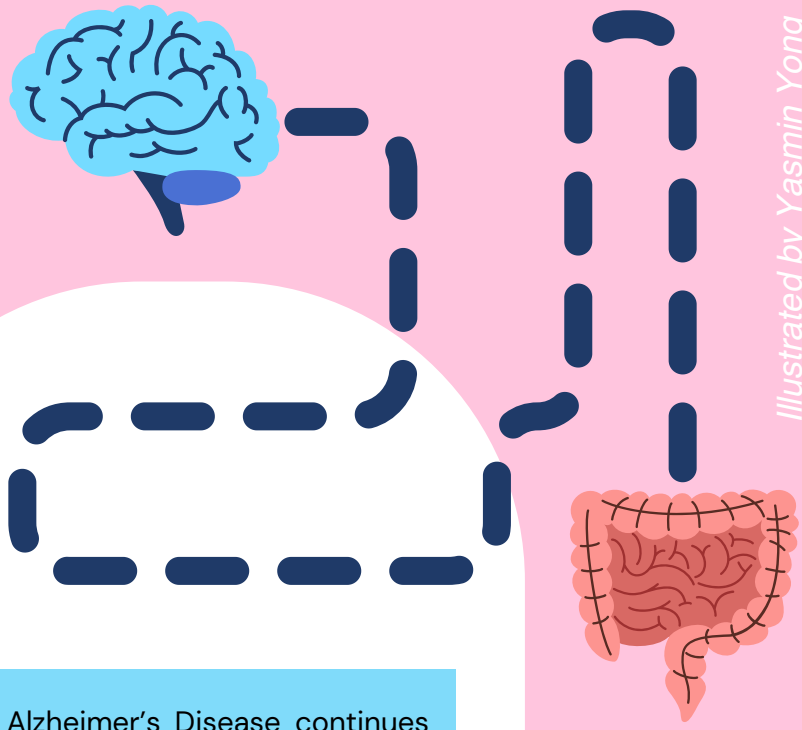
The expression of specific receptor proteins on immune cell surface membranes enables the cells to carry out specialised functions. Interestingly, senescent helper and cytotoxic T cells (TEMRA CD4+ and CD8+) tend to behave as natural killer (NK) cells instead by upregulating expression of typical NK receptors. NK cells are a type of cytotoxic cell in innate immunity. One of its main cell-destroying mechanisms proceeds via non-specific and antigen-independent release of lytic granules containing perforin and granzymes, which are proteins that can pierce the cell membrane and activate caspase-dependent apoptosis (cell death), respectively. The entire process of releasing perforin and granzymes is called degranulation. By assessing gene expression, Pereira et al. found that, compared to non-senescent CD8+ T cells, CD8+ TEMRA gene expression of T cell receptors (which bind to antigen-presenting ligands) were decreased whereas genes of NK receptors (NKRs) and genes involved in the NK cell cytotoxic pathway were elevated. Since each type of immune cell expresses a particular set of receptors that act as useful markers for identifying cell type and analysing cellular behaviour, looking into marker expression of TEMRA is fundamental for later cell function studies to further explore how genetic changes affect cellular functions. One widely used method is flow cytometry, which revealed that TEMRA CD8+ T cells express a significant number of NKRs, including degranulation marker CD107a, which is a NK-cell protein suggested to protect itself from damages by perforin and granzymes. Ongoing research held by Luciana Covre et al. at the Akbar Lab at UCL cocultured CD8+ TEMRA with fibroblasts (connective tissue cells) and looked into the killing effect, which indicated that CD8+ TEMRA did profoundly kill cells in NK-cell-mediated manner. Later studies have shown that CD4+ TEMRA cells also carry the same transformation. This finding is astonishing, as the paradigm of CD4+ T cells is no longer restrained to those "helper" functions outlined above, and somewhat carries "killer" roles, recognising antigen-presenting cells, activating cytotoxic cells, and introducing immune memory.

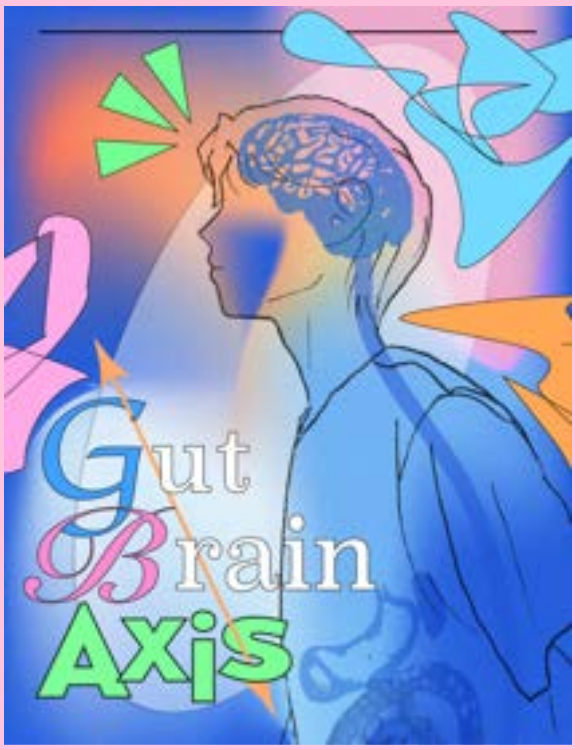
Pathways inducing immunosenescence have attracted great interest amongst immunologists; particularly, one sestrin-dependent pathway is well-established.

Lanna et al. suggested that T cell senescence can be induced by activation of sestrin, a stress-sensing protein. Active sestrin binds to three groups of MAPK proteins (a type of protein kinase), Erk, Jnk, and p38, forming a sestrin-dependent MAPK activation complex (sMAC). When sMAC is activated, Erk, Jnk, and p38 each boost distinct aspects of senescent T cells, such as increased DNA damage, decreased expression of T cell receptor components, and reduced telomerase activity. Therefore, it has been proposed that immunosenescence can be reversed by inhibiting sMAC, a potential pharmaceutical target.

Why bother to reverse immunosenescence? To answer this, we need to look into interactions between senescent T cells and tissue microenvironments. When tissues age, several proinflammatory markers, known as senescence-associated secretory phenotypes (SASPs), are released. The pool of SASPs is postulated to induce expression of both NKR in TEMRA cells and NK ligands in tissues. TEMRA cells begin to indiscriminately destroy any tissue cells that express NK ligands. Moreover, the killing from TEMRA cells further secrete more SASPs, accumulation of which can recruit other immune cells and lead to chronic inflammation. This is unfortunately a vicious loop, which eventually results in high level of proinflammatory markers in blood and tissue microenvironment, a phenomenon called inflammaging. Plentiful evidence suggests that inflammaging is a strong risk factor for various age-related diseases, such as cardiovascular diseases, cancer, dementia, and chronic kidney disease. However, the pathology remains unclear.

Senescent T cells undergo changes and form a destructive inflammatory burden in ageing individuals, despite their capability of eliminating senescent non-immune and cancerous cells to mitigate tissue damage and malignancy, respectively. Reversing T cell senescence remains a challenge,and the pathological roles of the "fallen angels" in age-related diseases are yet to be elucidated. The proposed pathway of sMAC formation suggests that sestrin and MAPK proteins can be potential pharmaceutical targets to reverse T-cell senescence and relieve inflammaging.





Illustrated by Yasmin Yong

Alzheimer's Disease continues to stand as a pressing and enigmatic global health concern. It is characterised by the accumulation of extracellular β-amyloid and intracellular tau protein deposits, which leads to synapse loss and neuronal death. However, the pathophysiological mechanism remains largely unknown, hindering the development of much-needed treatments and cures.

Interestingly, recent progress in scientific research has brought forth new advances in our understanding of this disease. Contrary to prior belief, the causes of Alzheimer's are not limited to the brain. New theories suggest origins from other parts of the body. Notably, current findings indicate an intricate relationship exists between the gut and the brain, where complexities within the gut microbiome directly impact brain health.

So, how are the gut and brain linked?

There is a microbiota-gut-brain axis consisting of bidirectional neural and metabolic pathways. Certain bacteria are believed to directly interact with the mechanisms of behaviour and cognition through this axis. Our gut microbiome is a complex ecosystem of 100 trillion bacteria. If there is dysbiosis, imbalance within the gut can manifest issues within the brain.

Gut bacteria and neurodegeneration

When our body is infected, or injured, it responds with inflammation, a natural defence that involves our organs and tissues. However, this immune response is also seen in the brain and the spinal cord, and is known as neuroinflammation. This type of inflammation is significantly associated with detrimental decline in cognitive functioning, from thinking to memory, as well as neurodegenerative diseases.

Inside our brain, there are special immune cells called microglia that act as a defense system. Via homeostasis, they maintain a healthy brain environment and defend against attacks by foreign molecules–either by phagocytic action or the release of proinflammatory cytokines. If microglia are sustained in their active state for too long, defined as an amplified inflammatory response, this can lead to neuronal degeneration, build-up of amyloid deposition, and even brain shrinkage. These pathological changes are often seen as we get older, and are strongly correlated with Alzheimer's Disease.

Yasmin Yong

The Gut-Brain Dialogue

Understanding our Microbiome's role in Alzheimer's

Eating foods with high fibre, like fruits and vegetables, allow certain gut bacteria to reduce inflammation by making and releasing short-chain fatty acids (SCFAs).

These SCFAs send signals through the gut-brain axis and have anti-inflammatory properties. Studies on ageing mice have supported this–more fibre in their diet increased SCFA concentration, which helped limit neuroinflammation. In another study, when SCFA mixtures were administered to post-stroke aged mice, they found a significant reduction in brain and gut inflammation, as well as improved behaviour. Gut bacteria are also involved in the formation of amyloid, which in turn potentially affects the amount of amyloid plaque in the brain. Interestingly, high levels of SCFAs seem to have a link to lower chances of Alzheimer's and similar memory problems. Therefore, SCFAs are believed to be linked to the reduced risk of Alzheimer's and other dementias.

In contrast, other bacteria in the gut can release lipopolysaccharides, which induce microglial activation and, thus, inflammation. Therefore, it is evident that different bacterial actions interplay in the mechanisms of neurodegenerative disorders.

Our genes can also play a part in forming the community of our gut bacteria. Recent research has found connections between specific gut bugs and genes linked to Alzheimer's risk, like the Apolipoprotein E ε4 gene. For instance, having lots of Collinsella bacteria in the gut might go along with having a gene that raises the risk of Alzheimer's (APOE risk), leading to more inflammation in the body.

What is the significance of all of this?

Our brain's health is influenced by a mix of our genes, gut bacteria, what we eat, and how our bodies process fats. This holistic approach to understanding and managing Alzheimer's has introduced potential ideas for new ways to prevent it. Nutrition experts believe high-fibre diets such as the Mediterranean Diet have neuroprotective properties and might protect our brains by defending against neuroinflammation.

As scientists conduct more research into this connection between our gut and brain, it is becoming increasingly apparent that what we eat doesn't just affect our bodies—it has an acute impact on our brains too. This poses an advancing area of study, and it is paving future avenues for scientists to explore with larger cohorts, harnessing a key to potentially transform the future of Alzheimer's Disease treatment and prevention.

PRION DISEASES

The Unusual Protein-Misfolding Diseases

Celine Tedja

Proteins are vital molecules in the machinery of cells. Therefore, having the correct and precise protein structures is crucial to ensuring properly functioning systems in the body. Even a slight error at such a molecular level can result in an undesirable complication. You have probably heard of the currently widely researched Alzheimer's and Parkinson's diseases, which are neurodegenerative disorders caused by the incorrect folding of proteins, resulting in irregular conformations of proteins. There are also less commonly known neurodegenerative disorders caused by protein misfolding, called prion diseases.

However, scientists are still studying these diseases in depth to unravel more information about them.

Prion diseases are **rare, fatal, and untreatable illnesses found in both humans and animals that cause progressive damage to the brain.** They occur when normal prion proteins, primarily found in the brain, fold into abnormal structures. The actual purpose of these prion proteins and the mechanism by which they can misfold have yet to be discovered. Some examples of prion diseases include Creutzfeldt-Jakob disease, bovine spongiform encephalopathy (BSE), Gerstmann–Sträussler–Scheinker syndrome (GSS), fatal familial insomnia (FFI), scrapie, chronic wasting disease, and kuru. These disorders can be sporadic (occurring occasionally), genetic (inherited or due to mutation), or acquired (transmitted).

The term

'prion'

was first coined in 1982 by Stanley Ben Prusiner, who worked at the Institute for Neurodegenerative Diseases at the University of California, San Francisco (UCSF). It is short for 'proteinaceous infectious particles.' He and his team were investigating the cause of scrapie disease. It was hypothesised that the agent was a virus; however, his research revealed that the purified sample contained no nucleic acid, which should have been present if the agent was a virus. Instead, a protein was found to be present in the sample. Prusiner won the 1997 Nobel Prize in Physiology or Medicine for his groundbreaking discovery.

The general mechanism that has been studied so far is that a naturally occurring prion protein called PrPC (Cellular Prion Protein) folds abnormally to form an irregular conformation called PrPSc (Scrapie Prion Protein). This may occur sporadically or due to genetic mutations of the genes regulating the protein. PrPSc can also be acquired through ingestion or other types of exposure since it is known to be infectious. Once present in the body, PrPSc will amplify the misfolding of other normal prion proteins. Furthermore, a group of PrPSc will accumulate and self-assemble to form insoluble aggregates (clumps) called amyloids. This phenomenon is called protein aggregation, which causes tissue damage and cell death. In this case, amyloids form vacuoles in the brain and neurons, thus making them spongy.

Prion diseases may be diagnosed in the same way as other brain disorders. Some methods include MRI (Magnetic Resonance Imaging) scans of the brain, collecting samples of fluid from the spinal cord, electroencephalograms, which analyse brain waves by placing electrodes on the scalp, and blood tests. They can also be confirmed by taking a sample of brain tissue during a biopsy or after death.

Illustrated by Naomi Chung

Currently, several research institutions are developing techniques to learn more about prion diseases. The Rocky Mountain Laboratories (RML) in Hamilton, Montana, have been culturing cerebral organoids (mini-brain models) in incubators to study how prion diseases affect the brain. Cerebral organoids are small groups of human brain cells derived from stem cells, and they recapitulate many aspects of the real, complex human brain. Another way to analyse protein misfolding is by using microplate readers capable of detecting fluorescence and certain fluorescent dyes. These dyes bind to amyloid aggregates, which results in an increased fluorescence signal. By monitoring the changes in fluorescence intensity over time, researchers can observe the kinetics of protein aggregation. These methods can therefore be used to potentially prevent advances in protein misfolding and develop therapies for prion diseases.

As a self-proclaimed picky eater, I have gone through many culinary experiences that have left me hungry for an answer to how my so-called 'fussiness' in food came to be. Family members have scolded me at the dinner table for cringing at the sight of vegetables whilst I've alternated between only a handful of preferred meals. This frustrating selectiveness towards food presents a puzzling occurrence in human behaviour–but how exactly do picky eating habits emerge?

Taste buds are a cluster of 50-100 taste bud receptor cells located on the tongue surface. Microvilli, also known as taste hairs, extend from these cell clusters and protrude through an opening called the taste pore. The taste hairs then interact with the chemical properties of food/tastants. This interaction causes taste receptor cells to undergo depolarization, resulting in a change in the electrical charge across a cell membrane. The depolarization sets off an action potential that proceeds to transmit sensory information to the gustatory (taste-sensing) cortex of our brain.

Classification of taste is moulded into five taste qualities: sweet, sour, salty, umami, and savoury. Taste bud cells are further classified into types I, II, III, and IV based on their structural and functional properties. Type I cells are dedicated to distinguishing salty tastes. Type II cells transduce a combination of sweet, umami and bitter tastes. Type III cells detect sour taste whilst Type IV taste cells are currently not known to possess taste functions.

The genetic basis of taste: how can genes lead to picky eaters?

Attitudes towards certain foods are far more extensive than just being 'fussy'; there's a reason picky eaters love the kids' section on a restaurant menu.

From a biological perspective, the foundation of picky eating essentially lies within genes.
Genes establish predetermined inclinations and aversions towards certain foods. On that account, it's common to see children have an evident dislike towards vegetables and a preference for sweets. TAS2R38 is a bitter taste receptor that modulates bitter perception. A study published by Frontiers in Genetics, aiming to explore genetic hallmarks in taste variation across databases, reported that TAS2R38 variants can determine taste sensitivity towards bitter foods.

TAS2R38 variation is induced by three single nucleotide polymorphisms (SNPs), a genetic variant at a single building block of DNA, that can lead to amino-acid alterations. These alterations can cause TAS2R38 variants to perceive taste differently upon consuming substances containing the chemical compound phenylthiocarbamide (PTC). Inheritance of a PTC taster gene is autosomal dominant. Hence, individuals with genotypes Tt and TT are often termed 'tasters,' exhibiting either high or intermediate sensitivity to bitter foods. Contrarily, the tt genotype is a recessive trait and is regarded as a "non-taster" – likely to not taste bitterness. Hence, broccoli, cabbage, Brussels sprouts and even alcohol might be the worst nightmare for some but decent for others.

Illustrated by Jordan Mooney

A GUIDE TO BEING A PICKY EATER

Azita Vatandost

On the opposite end, there's sweetness. Much like bitter perception, sweet perception also varies. TAS1R2 and TAS1R3 are the sweet taste receptors in humans. A study conducted by the QIMR Berghofer Medical Research Institute reported that certain SNPs can induce different perceptions of sweet intensity. This gives rise to the hypothesis that an inclination towards sugary foods could be correlated with having a weaker recognition of the sweet taste.

Can our taste buds change?

Similar to our other senses, our sense of taste diminishes with age. Our taste buds begin to shrink and are unable to regenerate as quickly, causing us to lose sensitivity to the five taste qualities. However, the natural decline does not occur until after our mid-50s and 60s. Thus, the shift from a bland palette typical of picky eaters to a slightly more diverse one can be better understood through a psychological lens.

A systematic review conducted by the USDA has shown that repeated exposure to a certain vegetable/fruit for 8-10 days shows an increase in the acceptability of certain foods in children. Although we cannot alter our genes, disliked foods may become appetising.

Ultimately, taste receptors' interaction with tastants and the food exposure we've had as children can be determinants of picky eating. Particular bitter and sweet receptors can classify us into genotypic categories whilst food exposure can develop potential tolerance to foods. Further studies have begun to highlight connections between the impact of social factors such as parenting habits and food presentation on picky eating. Therefore, could upbringing outweigh the influence of our genes on our taste selectivity? Which side of the nature versus nurture debate will take root in our eating habits?

WHEN SHOULD WE HAVE PROTEIN SHAKES AFTER THE GYM?

Jasmine Bains

If you've ever crossed paths with a gym rat, you're probably familiar with their immediate post-workout priority– ensuring they get enough protein. This usually involves the classic chicken and rice meal or a trusty protein shake.
But why do we need protein after a workout? How much do we require? And when should we consume it for maximal benefit?

When you exercise, microtears are formed in your muscle fibres. The extent of these tears depends on the length, intensity, and type of exercise performed. These microtears trigger muscle growth after exercise by stimulating muscle protein synthesis (MPS). This mechanism is the process by which your body is able to build new muscle proteins, composed of amino acids, to replace and repair damaged ones.

Therefore, when high-protein foods are consumed post-workout, they are broken down into amino acids during digestion by enzymes such as proteases in the pancreas. This increases the number of amino acids which are transported to your muscles where they are used in the growth and repair of muscle tissue. Some amino acids such as leucine are particularly important in stimulating MPS. Boosting protein intake after exercise not only helps to build muscle, which is usually the primary aim for gym enthusiasts, but also accelerates recovery by reducing muscle soreness. This allows for a quicker return to the gym and enables higher-intensity training, furthering muscle growth.

Illustrated by Naomi Chung

Many people drink their protein shakes as soon as they leave the gym, assuming this will maximise potential muscle growth. Nutritionists instead advocate for the consumption of high-protein sources within the anabolic window which spans from 30 minutes to 2 hours post-workout, which helps to maximise MPS.

However, research suggests that daily intake holds a greater significance than the precise timing right after a workout. This is because meeting daily protein requirements, especially for individuals engaged in regular exercise, ensures a consistent influx of amino acids necessary for muscle repair and growth throughout the day.

Various protein sources exhibit varying levels of efficacy at different time periods. For instance, protein shakes are believed to be most effective when consumed within a 20-minute window following exercise. During this time frame, both protein synthesis and muscle glycogen uptake are at their peak. Researchers emphasise that while protein is pivotal for promoting muscle growth, its effectiveness is further enhanced when consumed alongside other essential compounds such as carbohydrates. Carbohydrates play a crucial role in replenishing glycogen stores and facilitating recovery by providing the energy needed for MPS.

This is why many recovery drinks, like protein shakes, target a carbohydrate-to-protein ratio of 3:1 or 4:1, as 20g of protein is generally sufficient for most individuals post-workout. This insight also underscores the popularity of meals like chicken and rice among fitness enthusiasts for effective recovery.

In summary, post-workout protein consumption is essential for recovery and muscle growth, and is likely to provide maximal benefit when consumed within the anabolic window. However, maintaining a high protein intake daily will help to ensure consistency and further enhance results. While protein is important for muscle growth, it's equally crucial to recognize the significance of other elements like carbohydrates. They play a vital role in facilitating glycogen uptake, expediting the recovery process and contributing to more effective progress.

Exploring a New Theory

Elin Bonyadi

From being a means through which our subconscious thoughts are expressed, to being merely a product of random brain activity, people have long theorised about the purpose of dreams. With dreaming being so energetically costly to the brain, it is believed there must be a biologically important reason for it, although this has been difficult to elucidate.

However, an exciting new theory has recently been proposed to explain why we dream and why our dreams are so visual. This theory suggests our dreams help protect our visual perception abilities, which may otherwise be lost as we sleep. The brain has an incredible capacity for adaptation in response to changes in the environment – a concept known as neural plasticity. Brain regions that usually process a certain type of sensory input, such as visual information, can begin to respond to, or be "taken over" by, other sensory modalities if they no longer receive their usual input. These changes can occur much faster than once thought.

A particularly striking study by Merabet and colleagues in 2007 revealed that, after blindfolding normally-sighted individuals while they practised with tactile stimuli, a brain region usually associated with visual processing showed an increased response to tactile stimuli after less than just one hour. For neuroscientists David Eagleman and Don Vaughn, such findings led to the question: if the brain's visual regions can adapt so rapidly, why are they not completely taken over during sleep, when the brain is not receiving visual input from the outside world through the eyes? A new theory by Eagleman and Vaughn in 2021 proposed the reason this complete takeover of the visual regions does not occur overnight is due to dreaming. Their "Defensive Activation Theory" proposes that dreaming is evolution's way of preserving the visual processing abilities of the brain, by continuing to stimulate the visual regions during sleep.

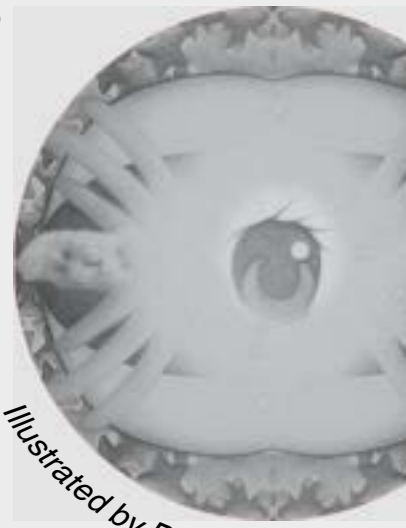
Most dreaming occurs during the REM (rapid eye movement) stage of sleep, characterised by dreams rich in visual content. In REM sleep, signals are sent specifically to the primary visual cortex from a region called the pons. This activation of specifically the primary visual cortex suggests dreams may occur to continue the stimulation of visual regions during sleep. According to the theory, this continued activation ensures these regions are not taken over by other sensory modalities, such as tactile or auditory, which are still active during sleep. Crucially, this theory would also explain the reduction in the proportion of time spent

in REM sleep across the lifespan, as the brain's capacity for plastic change decreases with age. With reduced plasticity, the threat of the visual areas being taken over is diminished, meaning longer periods of dreaming, and therefore REM sleep, are less necessary.

The Defensive Activation Theory also predicts that the more plastic an organism's brain, the more REM sleep it should have, as the visual regions of these brains would be at greater risk of takeover. In a study in 2021, Eagleman and Vaughn demonstrated evidence seemingly consistent with their theory: they found that greater plasticity was related to a greater proportion of sleep time spent in REM sleep across many primate species. The authors also noted that some medications used to treat depression inhibit dreaming and are frequently linked with visual problems. The authors suggest the reduction or interruption of dreaming caused by these medications may be the cause of these visual problems due to the takeover of the visual regions as a result of less REM sleep and, consequently, less dreaming.

In 2023, Knopper and Hansen published a response to the Defensive Activation Theory. While questioning the evidence the theory is based on due to recent findings that neither plasticity nor REM sleep decline with age, the authors did suggest a brain region which could underlie this mechanism: the locus coeruleus, due to its role in both REM sleep regulation and plasticity. Thus, they recommend further exploration of this region in relation to this theory.

Overall, the Defensive Activation Theory is an exciting new theory seeking to explain why we dream in pictures, a question which has long posed a mystery. However, there is currently a lack of research testing the theory's validity. Furthermore, the existing evidence by the theory's authors relies only on directionally consistent trends, which could have alternative explanations, and on indirect measures of visual cortex plasticity. Therefore, more research is needed to establish whether we have finally understood the purpose of dreaming.



Illustrated by Bella Marwick

I like what you like

The Whys and Hows of Fandoms

Savina Hui

Illustrated by Yasmin Yong

Art is a medium for communicating with other people, whether by sharing knowledge in an easily digestible format, or through bonding with other people over emotions evoked by a piece of media. In an era where the internet has simultaneously allowed the widespread broadcast of concerts, TV shows, and sports events, as well as the means for like-minded people to chat about their favoured media across time zones, communities of fans—colloquially known as fandoms—have cropped up in essentially every social media to ever exist.

Historically, fandoms have garnered questionable reputations, though that has gradually improved in recent years. Nonetheless, contrary to the doubt of naysayers, studies show that being part of a fandom is not only a natural outcome of intersubjectivity, but can also contribute to our mental and physical well-being.

Why do people form fandoms? It is for the very same reasons individuals gather to form communities. Humans are inherently social creatures who enjoy meeting others with perceived similarities to us. Due to affinity bias, people often seek out others with similar interests to themselves, therefore affirming themselves with consensual validation. By conversing with another person who appreciates the same anime, for example, one feels affirmed that they are 'correct' to enjoy that anime. They are more confident that their company will be appreciated, and hence feel more at ease around people who share similar interests.

The phenomenon of fandoms can be further explained by Social Identity Theory. It is a field developed by social psychologist Henri Tajfel, which analyses the connection between the individual and the community. Belonging to social groups helps people assign meaning to their lives and interpersonal relations. They redefine themselves based on characteristics shared between members of their community, hence gaining a sense of belonging and identity. Ultimately, being in a fandom is the same as being in any other community, only differing in that the individual's sense of belonging is centred around a common interest rather than alternatives such as living in the same neighbourhood.

Participating in fandoms can improve people's well-being, both mentally and physically. By partaking in activities that evoke positive emotions, one can potentially stave off stress and depression. This not only improves mental but also physical health, resulting in effects such as lower blood pressure and a stronger immune system.

Of course, it is also important to exercise and eat healthily—any health benefits you might get from engaging in fandoms will surely be eroded if you sit in front of a computer twenty-four seven.

Additionally, being in a fandom may incentivise one to create fan content. Expressing one's creativity through mediums such as fan art, fan edits and fanfiction can reduce stress, anxiety, and depression, evoking peace and calm with effects similar to that of meditation. It improves cognitive function by strengthening neural pathways of the hippocampus. Analysing TV shows and films can strengthen one's critical thinking, allowing one to overcome cognitive biases and make critical choices in real life. Of course, refusing to consider interpretations other than one's own may also cause someone to stumble into the pitfalls of perception bias in real life. As with many topics in real life, perhaps it will be worthwhile for fandom friends to discuss interpretations of their favourite media with an open and calm mind.

Considering the benefits above, it is safe to say that there is nothing inherently 'problematic' with fandoms. Nevertheless, like many communities, they are not immune to the presence of toxic individuals. This issue is especially prevalent online.

So, what does online toxicity encompass? Toxic behaviour often involves wielding offensive and humiliating words against other people in chatrooms and forums. Such actions can vary in severity, from degrading language to hate speech, or even culminate in cyberbullying.

The most intriguing aspect of such behaviour is that the perpetrators are often otherwise decent individuals in real life, who would never behave this way with people they meet face-to-face. The question then arises: why do they behave differently behind a screen? This can be explained by the online disinhibition effect, a term used to describe the anonymity and disconnect the internet affords people.

The distance of the world wide web allows people to don a mask, lowering their inhibitions such that they display behaviours inappropriate in real life. This is exacerbated by asynchronous communication–the time gap between one person sending a message and the recipient reading it, as well as the lack of visibility and eye contact between the two parties. They allow the sender to type incendiary messages without considering the recipient's reaction.

While the internet may appear divorced from real life, what happens online can still impact our daily lives. Undue harsh criticisms of TV shows and movies not only put off genuine fans, but also damage the confidence and reputation of the creator, especially if they are an artist posting content without the backing of a company. This is doubly true with regard to fan content, in which content creators share the fruits of their labour without compensation or pay.

Fandoms are meant to be a stress-free place to bond with people over a common passion. When faced with toxic fans, it is important to disengage, take a step back, and distance yourself from your fandom until the storm has passed. If your fandom is causing you undue stress, it is probably time to log off.

To conclude, it is not unusual for fandoms to be a crucial aspect of your interests and even your social life. However, like all other things, one must be careful not to overindulge in fandoms, lest it overtake real life with detrimental effects to your health and social circle.

The Psychology of Socialism: Are Humans Intrinsically Selfish?

Aphra Greenwood

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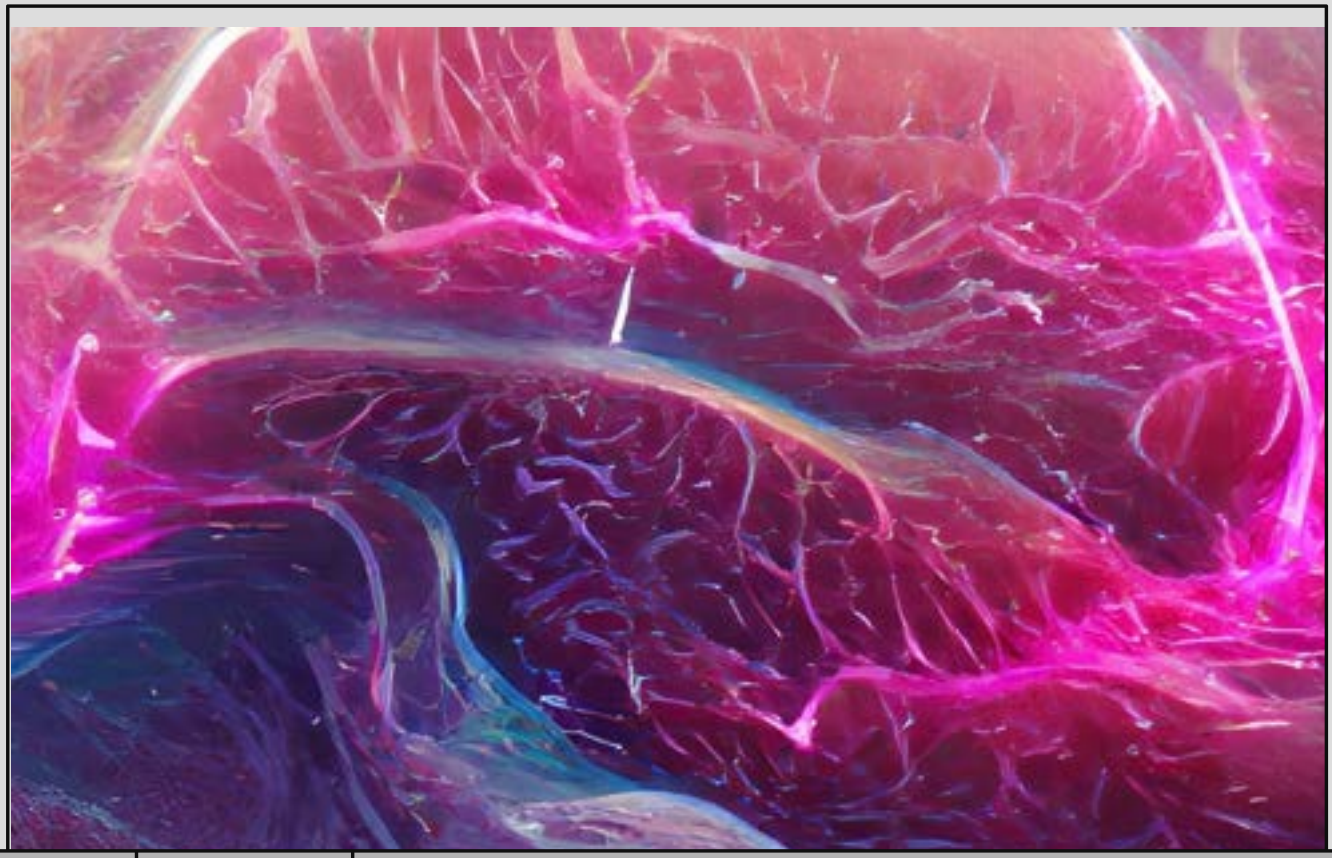

Page 1 | Words: 88 | *Illustrated by Bella Marwick*

Capitalist systems are based on self-interested behaviour and competition between individuals to make profit. It is often assumed that an intrinsic element of human nature leads to this structure– that humans naturally compete and put their individual needs first. But are humans selfish? Arguably, self-interested behaviour is a product of our competitive societal structure, rather than a fixed, innate human quality.

Socialism as a political system is based on the fair distribution of wealth, the sharing of property, and equality. These values can be viewed collectively as prosocial behaviours, which encompass cooperation, resource sharing, and helping others–behaviour by individuals for the good of the society as a whole. Altruism, or selflessness, is a key aspect of prosocial behaviour.

Socialism is often discounted for being idealistic and unrealistic. However, psychological and human behavioural ecology studies suggest that humans are predisposed to altruism. From infancy, humans try to help each other achieve their goals, including unfamiliar new people. Even before developing speech, infants pass objects to others, or point to things that somebody else is looking for. These findings put to question the widely held narrative that from infancy, humans are fundamentally selfish and focused on their own interests. Another study found that children are intrinsically motivated to help one another due to feelings of sympathy, and external rewards do not affect how much they help each other. This contradicts the capitalist narrative of humans being selfish and reward-oriented.

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Prosocial behaviour is observed in other species, such as our closest relatives, chimpanzees, but humans are more inclined to share resources, which is a particularly costly behaviour as it reduces individuals' resources. This indicates a uniqueness to human altruism, where people will make self-sacrifices for others. Humans also exhibit more altruism towards non-familial or non-genetically related members of their society, in comparison to chimpanzees. It is believed that the evolutionary mechanism behind human prosocial behaviour is feeling concerned for those we are interdependent with. As such, we want to help those in our wider social group, who depend on us and on whom we depend, instead of helping only those closely related. This underpins the ability of humans to cooperate on a large scale for the benefit of the group. An example of prosocial behaviour is the way people responded to the Covid-19 pandemic. A Russian psychosocial study found that prosocial behaviours such as volunteering, helping strangers, and following preventative measures to help the community were all associated with feelings of benevolence. This was seen across societies, where people worked together for the collective cause of preventing the spread of disease and protecting vulnerable people.

Logically, the question may arise that if humans innately behave altruistically and selflessly, why does the current capitalist system that thrives off greed and self-interest prevail? Human behaviour is plastic and people have the capacity to behave in numerous ways, despite innate tendencies. Behaviours arise from interactions between

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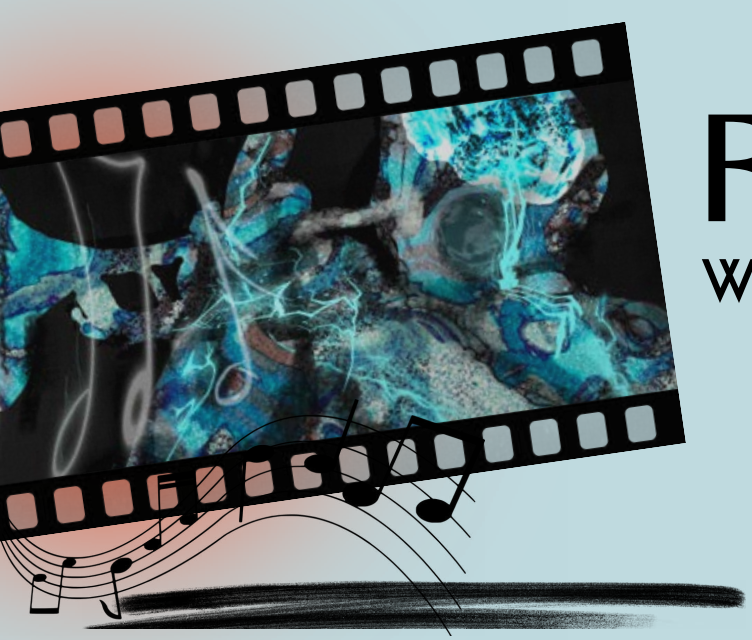
our minds, environmental circumstances, and social norms. A study in Bangladesh into the anthropology of altruism found that perceived feelings of cohesion or closeness are associated with altruism, rather than genetics or familial relationships. This indicates that we have to feel close to and trust one another in order to promote altruistic behaviour. A cross-cultural study found that prosocial behaviour develops in response to social norms. That is to say, in a society where sharing, cooperation, and helping others are normalised, these behaviours will be seen more often in children and adults. This highlights the importance of our attitudes towards human nature and whether or not we are altruistic; by shaping our beliefs and norms we can influence the level of prosocial behaviour in our society.

Capitalism promotes a cynical psychology in which people are believed to be primarily self-interested and selfish. A key feature of capitalism is that it claims that alternative systems do not work. Changing the discourse around human self-interest by replacing it with encouragement of altruism and resource sharing could increase prosocial behaviour. Consequently, in a socialist political system, our social environment would assist cooperative behaviour and community success.



Feeling Jazzy

What Improvisation Does to the Brain

Jung Woo Kim

Your tenor saxophone glistens gold in the dim lights of the jazz bar. You and your band are playing the last few notes of the main melody, and you begin to take your solo. You play a melody which soars over the familiar chord changes, weaving in and out of the key like a needle through cloth. You finish with a trill on a high E flat, and the crowd applauds as the trumpet player picks up right where you left off, beginning their own solo.

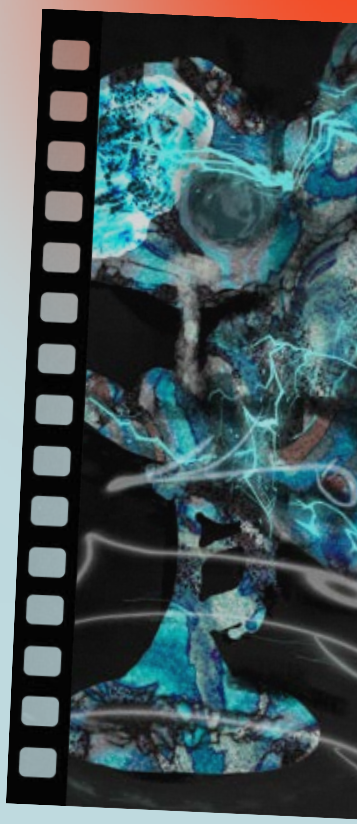
The question is: what on earth was going through your head?

Jazz musicians differ from classically-trained musicians in that they take solos, an improvisational section where players compose a melody on the fly. The best players draw from their own practice and the repertoire of great jazz musicians before them, all the while listening to the rest of the band and responding in real time. In other words, jazz solos require both a high level of technical ability and creativity. Though this has a steep learning curve, over time musicians gain confidence and learn to get 'into the zone' during a solo, feeling a simultaneous sense of effortlessness and intense focus. Sometimes, they forget that time is passing, and the rest of the world slips from view, leaving only them, their instrument, and their accompanying band. This feeling has a name, coined by psychologist Mihály Csíkszentmihályi, called 'flow.'

Think back to a time when you were completely absorbed in some activity, just difficult enough to keep you hyper-focused and lost in the intrinsic thrill of the activity. That is the flow state, and it can arise from sports to video games, from painting to, of course, playing music. Put simply, it is a state of mind where your attention is held by some engaging, enjoyable task.

Csíkszentmihályi states that there are six components to achieving the flow state: intense focus on the present, synthesis of action and consciousness, loss of self-consciousness, a sense of control, a distorted perception of time, and an intrinsic motivation to experience the activity. He also claims that achieving the flow state results in a greater sense of satisfaction for the individual experiencing it.

This link between the flow state and jazz improvisation was studied by Vergara et al. in 2021 by using functional Magnetic Resonance Imaging (fMRI) techniques on the brain. Jazz improvisation was of particular interest to these researchers as a model to study spontaneous creativity. This is because jazz musicians do not get to revise their solos once they've played them, compared to outputs that are not made in real-time, like writing or painting. It was theorised that creativity involved an interplay between the free generation of ideas and the self-evaluation of ideas.



Notably, the former is governed by a brain network called the Default Mode Network (DMN), and the latter by the Executive Control Network (ECN). You can think of the first as the daydreamer, while the second is the director who decides which of their thoughts will be translated into action. By taking fMRI readings of 12 professional jazz pianists, they found the areas of the brain that are most active during improvisation.

The researchers recorded the brain activity of the pianists when playing pre-learned music.
This allows them to determine what areas are functioning as the pianists play. Then, they recorded their brain activity when improvising a novel melody over some chord changes on the piano, with their voice, and in their imagination.

By subtracting the pre-learned piano brain activity from the improvised piano brain activity, they found that activity in the DMN (self-expression and idea
generation) was increased, while activity in the ECN (idea monitoring and evaluation) was decreased. This was replicated in the imagined and vocalised improvisation experiments.

In other words, jazz improvisation is linked to decreased inhibition and increased mind-wandering, regulated by the interactions between multiple brain networks which may also reflect a state of flow.

What does this mean for jazz musicians? Firstly, accessing the flow state may be key to pulling off a good solo. This means practising in order to improve your technical ability until playing becomes automatic. On top of that, you'll need to take creative risks and play without excessive self-censoring. Ultimately, if you ever find yourself taking a jazz solo: just go with the flow.

Illustrated by Jordan Mooney

Musical Mind

Katie Kavanagh

Illustrated by Qiwen Liu

Now Playing

Music is a part of everyone's life, playing a versatile role and affecting each person uniquely. It is a pastime, a career, and a mood regulator. But could it be more than just the background character in our memories? Could it have the ability to slow the loss of these memories, even for someone with a memory disorder? Could it prevent the development of these memory disorders altogether?

Alzheimer's Disease (AD) is the most common form of dementia (memory disorder) in the world, affecting approximately 55 million people worldwide. Despite the high number of people suffering from Alzheimer's disease worldwide, treatments are limited and there is a desperate need for new advancements. Approximately £17.3 million is spent in the UK on Alzheimer's research annually. Despite this significant funding, only 10% of pharmacological treatments currently reach their desired effects, often causing unwanted physical side effects, and increasing distress and confusion for patients.

AD is caused by nervous system degeneration, largely due to abnormal accumulation of misfolded proteins β-amyloid and tau within specific regions of the brain. This build-up of proteins causes plaques and tangles to form within the hippocampal formation which decreases neurotransmitter numbers, in particular acetylcholine, inducing memory and cognitive impairments.

However, the pathological effects of AD are not uniform or equal across different brain regions.
The brain areas involved in music cognition are theorised to deteriorate more slowly than their non-musical counterparts. This has led to the exploration of music as a therapeutic agent to delay symptom progression in those already living with AD, but also to prevent disease onset.

Memory loss is the main symptom associated with AD, however, patients also suffer from physical symptoms such as difficulty swallowing. Known as dysphagia, difficulty swallowing is experienced by 13-57% of Alzheimer's patients, making mealtimes stressful and reducing food intake, which can lead to malnutrition. Accompanying dysphagia is aspiration which is the intake of food, liquid, or saliva into the lungs, and can lead to pneumonia–the most common cause of death for those with Alzheimer's.

A study carried out by Columbia Healthcare Centre featured Alzheimer's patients who received personalised playlists with songs from their childhood that hold significant meaning to them. They listened to these playlists for 30 minutes before dinner and their food intake was recorded with and without intervention. The average food intake increased from 41.4% to 71.4% with this music intervention, the 30% increase indicating a decrease of dysphagia, aspiration, and distress. This simple addition to patients' daily routine is an amazing alternative to Percutaneous Endoscopic Gastrostomy (PEG), known as tube feeding, which removes independence and normality from patients' lives.

While listening to music can decrease AD symptomatology, it has also been shown that playing a musical instrument can decrease the chance of it developing. A survey to explore the possibility of prevention was carried out by Loyola University Chicago. It consisted of 23 orchestral musicians who were aged 65 years and upwards, the age at which 10% of the population are expected to develop Alzheimer's. Their musical background, family history and health were all taken into account and they were screened for Alzheimer's. Results showed that none of the musicians had developed Alzheimer's despite familial and age-related prevalence.

In several cases it has been demonstrated that patients in the moderate to severe stages of Alzheimer's, experiencing severe cognitive impairments, still possess the ability to learn and play songs, demonstrating intact musical procedural memory. Playing a musical instrument has been shown to increase cognitive ability through enhanced neuronal communication between the left and right hemispheres of the brain, which causes positive effects on learning, memory, fine motor skills, verbal reasoning, and non-verbal reasoning.

It is theorised that playing an instrument over a long period of time can lead to plastic changes such as the rapid unmasking of existing connections between neurons and even the establishment of new connections. The functional and structural changes in response to music have been observed through neuroimaging techniques such as fMRI.

Despite such evidence, the effect of music on memory disorders is not yet well-established, and requires significantly more research and funding to solidify music's role in the treatment and prevention of AD. Music could potentially be the affordable, easy-to-use, and remarkably versatile remedy we've been searching for, offering a refreshing alternative to traditional pharmaceutical treatments for those navigating the challenges of dementia.

Mini Brains

Can they be grown in a dish function like a human brain?

Melanie Bonyadi

"Mini brains," or brain organoids, are a **3D multicellular tissue generated from human-derived pluripotent stem cells** that have been reprogrammed to resemble the human brain. To do this, human cells, such as skin cells, are taken from a patient and reprogrammed by specific transcription factors into induced pluripotent stem cells, which can differentiate into any cell type. These stem cells are then induced to differentiate into neural stem cells, which can produce many of the cell types found in the brain and can then be aggregated together to form 3D structures that can physiologically respond to signals in a similar way to the human brain. At this point, the organoids can also form structures such as neurons that can be representative of specific brain regions.

Given the structural and functional complexity of the brain, the extent to which brain organoids can develop structures in the same way as a human brain remains elusive. A study by Trujillo and colleagues reported electrophysiological waves of activity in brain organoids and found alternating periods of quiescence (inactivity) and synchronised oscillatory activity. Even though this pattern of activity does not demonstrate the full complexity of adult brain activity, it does resemble electrical activity observed in preterm human infants, hence demonstrating the potential for brain organoids to exhibit human-like electrical activity. Furthermore, these synchronous waves of activity could possibly indicate a functional neuronal network and given that this type of activity is important for the flow of information between different brain regions, these results seem promising.

Subsequently, this leads us to question whether these brain organoids could be conscious.

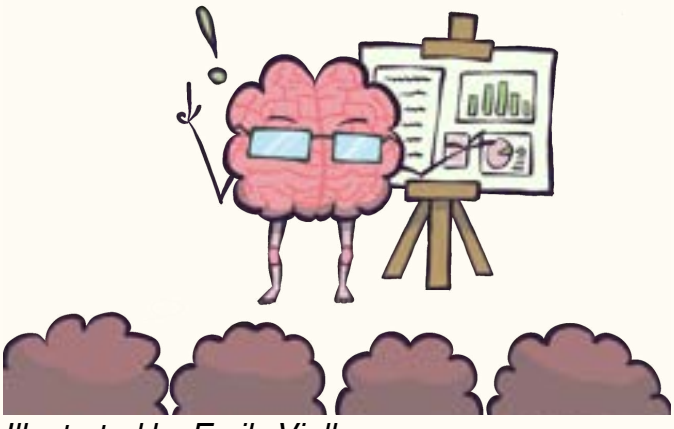
This is a difficult question to answer as there is often ambiguity concerning the definition of consciousness. One approach for assessing consciousness in brain organoids would involve stimulating them with a pulse of energy. In theory, if the organoids are "conscious," they should produce an electrical "echo"; an unconscious organoid would remain unresponsive to this stimulation. However, this type of experiment has not been conducted in brain organoids to date. Another way to evaluate consciousness in brain organoids could be to measure their responsiveness to light stimuli.

For example, Quadrato and colleagues found that brain organoids cultured for an extended period of time generated photoreceptor-like cells that have proteins that are required to respond to light. These organoids also showed signs of neuron firing, which normally indicates communication between neurons, following light exposure. Although these results may seem promising, there is still insufficient evidence to ascertain whether brain organoids can be deemed as "conscious," as the organoids would be unlikely to be able to process visual information from the light.

Therefore, many neurobiologists do not currently think that brain organoids are capable of being conscious.

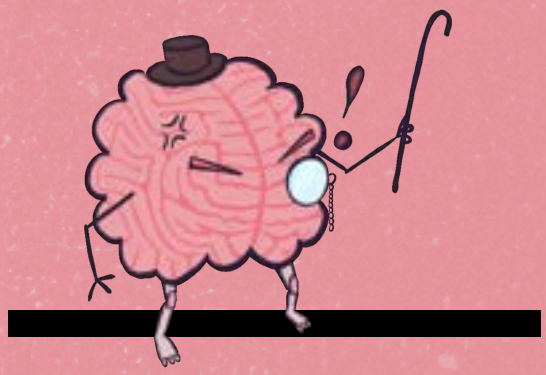
Overall, human-derived brain organoids can be a more useful model for studying diseases than using animal models or 2D human brain models, as organoids more closely resemble human brain development. Organoids can therefore be used to study diseases, such as for identifying how risk factors of a disease are linked to cellular phenotypes, understanding how pathogenic mutations can affect tissues, and screening potential therapies.

For example, Mohamed and colleagues found that midbrain organoids derived from human cells in patients with a mutation in the SNCA gene (which is known to be a risk factor for Parkinson's disease) had increased levels of aggregates that are normally seen in human Parkinson's patients.



Illustrated by Emily Vialls

This suggests that using brain organoids as a model for Parkinson's disease could be vital for studying the pathogenesis of the disease. Having said this, there are still ethical implications that should be considered when using brain organoids in research. For example, using human cells to create organoids can be an ethical issue as it is important that the donors give consent and know what research their cells are being used in. In addition, the consequences of transplanting organoids into humans or animals would need to be considered.



For example, one experiment found that brain organoids implanted in rats led to their integration into the rat's brain and appeared to affect its cognitive abilities, which raises issues about humanising animal brains.

Therefore, despite these potential shortcomings, brain organoids the size of a sesame seed could revolutionise research and understanding of brain diseases and provide a platform for testing potential treatments for such diseases in the future.

Neuroepigenetics

How the Past Affects the Present

There's long been debate on whether a person owes their identity to their genetic makeup or their life experiences–the classic "Nature versus Nurture" argument. However, the emerging field of neuroepigenetics adds more nuance and complexity to this debate, suggesting that traumas experienced by our ancestors may be inherited by us and explain our own behaviour.

Basic Principles

Neuroepigenetics is the intersection between neuroscience and epigenetics. The discipline studies heritable changes in gene expression without modification to the genetic code, examining how this affects the cells of the central nervous system (CNS) and the subsequent implications for behaviour and brain function.

The mechanisms for changes in gene expression involve DNA methylation and changes in chromatin structure via histone modification. When methyl groups are added to CpG islands of promoter regions, it prevents the binding of the transcriptional factors to DNA leading to suppressed gene expression. Histone modifications can lead to chromatin being packaged densely so the gene is physically inaccessible to transcription factors, once again leading to suppression or for chromatin to be loose and easily accessible leading to upregulation of a gene. It's thought a traumatic event can trigger these mechanisms, affecting specific combinations of an organism's genes, resulting in a behavioural change.

Past – Present Interaction

Traumatic events aren't only confined to war experiences but can be physical, sexual, and verbal violence, abuse, neglect, and humiliation – experiences that can affect any person. Trauma's effects vary depending on the age it was experienced and the duration. Researchers, including Isabelle Mansuy, studied these effects in mice exposed to chronic and unpredictable maternal separation from postnatal day 1 to 14. They found the mice exhibited depressive-like behaviours and changes in response to aversion environments in adulthood. The offspring of males subjected to maternal separation also expressed these behavioural changes. Furthermore, there was a change in the profile of DNA methylation in promoter regions of genes in the sperm cells of separated males with changes in DNA methylation in the brains of the offspring.

Illustrated by Luli Fukukawa

So, what does this mean? The 'trauma' experienced by the mice in early childhood caused a behavioural change, potentially linked to epigenetic changes in gene expression. These changes were passed onto the offspring of separated male mice, leading to similar behaviour being exhibited by their offspring despite not experiencing maternal separation themselves.

This highlights another important aspect of transgenerational epigenetic transmission; epigenetic changes affecting the reproductive cells may be responsible for the manifestation of symptoms in offspring.

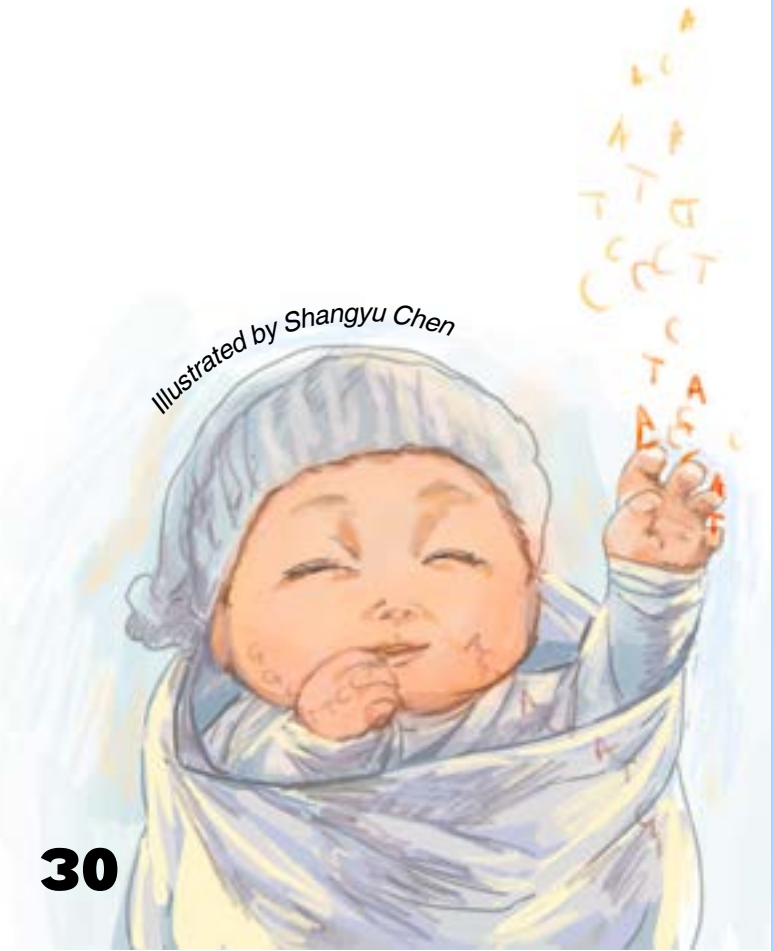
The Future

Large-scale genome-wide associated studies have identified over 100 loci associated with different neuropsychiatric and neurodegenerative disorders. Epigenetic changes stemming from traumatic events are believed to affect these regions and therefore play a role in these disorders. Considering this, various epigenome targeting drugs are in clinical trials with hopes of reversing environmentally induced epigenetic changes to the CNS. However, epidrugs aren't yet ready for widespread clinical use due to the susceptibility of the CNS to their "genotoxicity, low stability, multi-targeted and multi-cellular effects." Moreover, with the still limited understanding of neuroepigenetics and its implications, a linking of observations from multiple brain regions and large populations of people to cell-type-specific analysis is required. Ultimately, neuroepigenetic research may not only be the key to understanding who we are and our behaviour, but also provide hope for more effective treatment of neuropsychiatric and neurodegenerative disorders.

UK's Newborn Genomes Programme

Should We Know a Baby's Future?

Yunning Yuan



Illustrated by Shangyu Chen

"Every year 3,000+ babies could benefit from life-saving or life-changing interventions thanks to whole genome sequencing (WGS)." This is a statement asserted by Genomics England in its vision document for the Newborn Genomes Programme (NGP), launched in December 2021. Genomic medicine, which describes the use of information from a human's genome to guide clinical care, has been put under the spotlight for its enormous potential to diagnose diseases, and the concerns about whether predicting a baby's future is morally right. In this article, I will discuss the technical advantages as well as the ethical challenges of the NGP program to argue why and how we should use WGS for newborn screening.

As we enter the post-genomic era, WGS technology has become cheaper and faster than ever and has begun to change the practice of screening tests for babies. The Newborn Genomes Program (NGP) is a UK-based national research project which has started recruitment in 2023 to sequence the genomes of over 100,000 newborns. Its aim is to investigate the benefits, challenges, and practicality of WGS in early diagnosis and treatments of diseases, as well as the feasibility of using this data to drive scientific research. Currently in the UK, blood spot tests are offered to all babies to check for 9 specific monogenic conditions. Some suggest that we should expand the screening criteria to include additional genetic conditions, and that WGS could be an effective way of doing this. Revealing the individual genetic makeup can be used to calculate the risk of various diseases, thus allowing earlier supervision as well as personalized treatment.

However, others argue that using WGS to look for a broad range of conditions in healthy babies may not be reasonable due to limitations of the technology and possible unsolicited results. According to a 2020 study, the genome sequencing technology for detecting errors of metabolism at birth had a sensitivity of 88% and specificity of 98%, which is not sufficiently accurate to become the primary screening method.

If the risk of developing diseases calculated by WGS data analysis is not conclusive enough, should it be returned to pre-symptomatic babies? Furthermore, interpreting the WGS results is difficult since various non-treatable diseases and complicated pathogenesis are not well understood yet. These findings may vary greatly in clinical significance and actionability – should results be given to patients when they are not preventable or extremely difficult to cure? How would this impact the family's dynamic? In terms of unanticipated results, there are certain circumstances where a conflict may arise between the child's rights and the family's interest. As newborns lack the legal capacity to consent, their guardians are decision-makers of treatments. The controversies now centre on how WGS results should be managed and returned to benefit the family as well as protect the baby's rights.

Although WGS may generate some clinically non-relevant or non-actionable outcomes, it is still the most efficient tool to detect rare pathogenic variants. On average, it takes 6 years from the initial symptoms to the accurate diagnosis of rare diseases when using conventional approaches. WGS could give insights on the genetic disease within a few days, which allows suitable treatments to be delivered as soon as possible. In addition, WGS provides the best means of identifying rare causal variants of polygenetic conditions like autism, connective tissue disorders and cardiomyopathies. The accuracy could be further improved by combining with other screening tests to avoid false-positive results.

While there are concerns about letting healthy children wait to develop an illness, I would argue that genetics alone cannot dictate their destiny, and lifestyle pulls the trigger for most multifactorial diseases. Knowledge about a high risk for a disease can encourage parents to adopt lifestyle modifications to mitigate the risks. Most importantly, the focus should always be placed on conclusive findings where interventions exist to potentially reduce harm. For individual families, diagnosis of genetic conditions by WGS screening and early treatment is not only associated with the physical comfort for the child but also closely linked to the parents' spiritual pursuit of bringing up healthy offspring.

For the development of society, building a genomics data infrastructure through broad WGS data collection would help advance genetic research, transform personalized medicine, and stimulate a vibrant genomics industry, which would ultimately bring long-term benefits to the healthcare infrastructure and population.

In order to decide what kinds of results should be returned, we must consider the adequate protection of child's rights. According to the Convention on the Rights of the Child (CRC), a child has the following rights related to the screening tests: survival, respect of the view, privacy, and non-discrimination, with provisions for extreme circumstances such as abandonment or abuse. Although parents have the duty and ability to make medical decisions, screening results should be returned on the basis of the child's best interest. Children could grow up to have the capacity to understand genetic information and decision making. Adolescents should have access to their genetic data and have rights to choose appropriate therapies. Personal sequencing data can be kept for future access, but privacy protection policies must be made to ensure the safe storage of DNA information and prevent it from being used for commercial purposes. Furthermore, sensitive findings like disorders in sex development, ancestry and intellectual capacity which have less clinical relevance should not be informed or retained.

In conclusion, WGS can effectively boost early disease diagnoses for babies, but the child's rights and interests should always be given due weight when returning the medical findings. The application of WGS to newborn screening is a promising trend to improve supportive experience for the baby and the family.

What Lies Beyond XX and XY?

Micah Gerstner

Sex is Simple – Right?

Historically, there have been two distinct categories of sex, male and female. This distinction can be found in ancient religious and historical texts, and has endured to even today, with the definition taught to each person in school. A male is someone who has a penis and testes, with XY chromosomes. Usually they have other traits too, like an adam's apple and a deep voice. Males also tend to be taller on average and have more body hair than females. On the other hand, females have a vagina, ovaries, breasts, and XX chromosomes. Their hormonal profiles are largely determined by FSH and estradiol, which change based on their age: a menopausal woman has a different hormonal profile than girls before and after puberty.

Within sexes, there is a lot of variation in physical characteristics, yet we still feel confident in describing people as male or female. Sex hasn't always been so simple. People with indeterminate genitalia and sex expression similarly date back to ancient texts. The Sumerian text of Enki and Ninmah shows Ninmah creating one who is "without penis or vagina." Early rabbinic literature, namely the Mishnah in a section called the Bikkurim, describes laws around androgynous and tumtum, persons of indeterminate sex and concealed genitalia respectively. Even the Hellenes had Hermaphroditus, a son of the gods with male and female features after the gods caused him and a nymph to merge into one being. Throughout history, humans have been looking for explanations as to how people can appear to be of multiple sexes or of none, and how these people should be treated.

How does sex develop?

Sexual differentiation begins within the first few months of foetal development. Before any sex organs are developed, the gonad is bipotential – with the right stimulus, it can develop into either ovaries or testes. In most cases, if the genes in the sex-determining region of the Y chromosome (SRY) are present and activate during the 6th week of development, a cascade of chemical reactions will stimulate the gonad to develop into testes and suppress the development of the female reproductive system. If the SRY is absent, either through mutation or the presence of two X chromosomes, the female reproductive system will develop instead.

For most people, this process goes undisturbed and they have a normal sex expression.

Figures are inconclusive about how many infants are born with atypical sex expression, though a recent review suggests 0.02–0.05%. However, sex development doesn't stop at birth. Sex continues to develop during puberty, with the expression of secondary sex characteristics and eventually culminating in sexual maturity. This phase usually involves hormonal expression. Atypical sex expression may present as delayed or incomplete

puberty, or even traits from the opposite sex, such as breast development in boys or virilisation in girls. These individuals may appear to have typical genitalia and have been assigned a specific sex, but instead have a disorder of sex development that wasn't identified at birth.

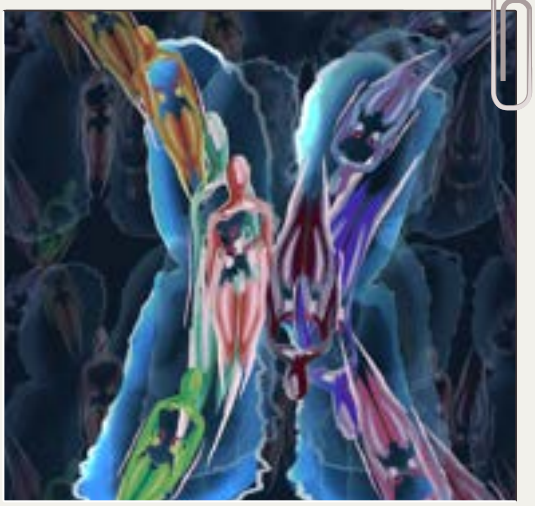
One of the earliest reviews on sexual non-dimorphism suggested that the incidence

rate of live births is around 1.7%, however a letter to the editor suggested that it might instead be 0.37% because of issues surrounding the figures used. In each of the studies regarding the prevalence of these conditions, the researchers acknowledge

that there is a lack of data on intersex individuals and that each figure may include different conditions for their estimation.

Differences in Sex Development (DSD)

DSDs are a broad group of conditions, which are poorly defined in medical literature due to a lack of standardisation. However, DSDs are grouped based on the characteristics they tend to share: is it caused by chromosomal variation? Is it due to sex hormone insensitivity? Witchel suggests that DSDs can be classified into categories such as XX DSD, XY DSD, Sex Chromosome DSD, Gonadal Development DSD, Persistent Mullerian DSD, and malformation DSD. These conditions occur due to random chance mutations, recessive genes, or errors during meiosis or mitosis. Perhaps the most well known of these conditions stem from chromosomal variation. Klinefelter syndrome is a condition in which more than one X chromosome is present in a phenotypic male, such as XXY. They may have a smaller phallus and testes at birth, or it may present as smaller during puberty. It is also common for these people to develop gynecomastia, enlargement of male breasts, during puberty. A similar condition exists in phenotypic females known as Turner syndrome. These individuals lack an X chromosome and are usually described as simply X or XO. They tend to have an increased risk of cardiovascular and neurocognitive disorders, as well as having "streak gonads," or connective tissue in place of ovaries which typically renders them infertile.

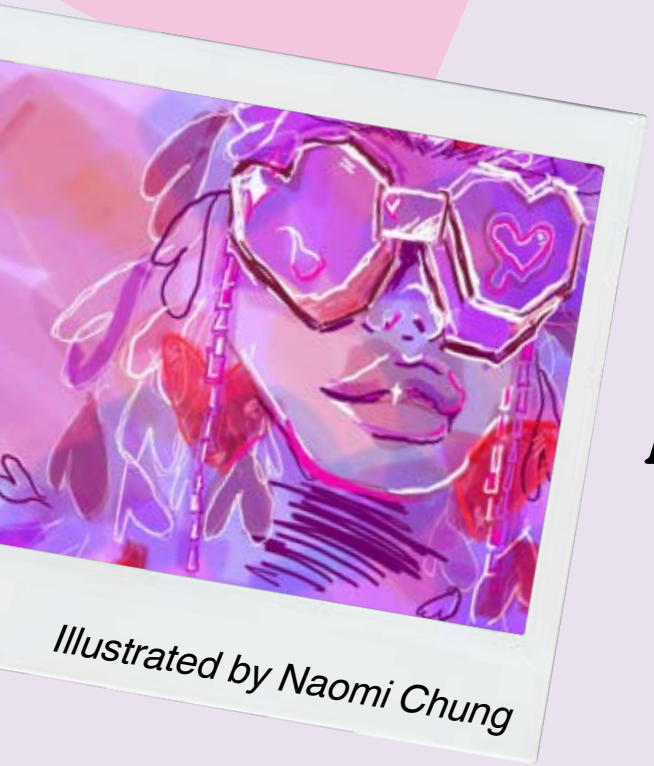


Illustrated by Luli Fukukawa

Life Beyond XX and XY

People with intersex conditions have always been and will continue to be a part of our societies for years to come. As medicine continues to develop, researchers will be better equipped to understand these conditions and what they mean for us as humans. The existence of these individuals suggests that a binary category of sex isn't accurate to the entire human experience. Certainly, these classifications have been helpful both socially and medically, but perhaps it's time to reexamine the importance humanity places on sex.

After all, how do intersex people fit into a society with binary male and female dimorphism as the norm? What about the law regarding sex? Should intersex individuals be forced into a category that doesn't reflect their biological reality, or be excluded from single-sex spaces? Should they have their genitalia corrected via surgery to fit into this binary society? These are questions that we will have to contend with for the upcoming decades as we continue to learn more about these conditions, both from research about them and listening to the people who have them.



Illustrated by Naomi Chung

Haowen Xue

Do Epigenetics link with Myopia?

Myopia, a condition commonly known as "refractive error", is caused by the focusing of light rays in front of the retina (instead of on it) due to the eyeball being too long. Nearly 1 in 5 teenagers are diagnosed as being myopic, and this is becoming an increasingly prevalent disorder globally. Therefore, it is important that we understand its basic mechanism and the ways to prevent the further progression of myopia. While it is obvious that genetics is a major factor in myopia pathogenesis, factors of epigenetics (the study of changes in phenotype due to changes in gene expression, rather than changes in the DNA base sequence) are also significant. This article will discuss how epigenetics may increase the risk of developing myopia.

Studies have revealed that epigenetics plays a critical pathogenic role in myopia progression. A recent paper has shown that more than fifteen gene loci (physical locations of genes on a chromosome) have been identified as being hotspots of DNA methylation in highly myopic people. DNA methylation is the process by which methyl groups are added to the DNA, causing transcription to be repressed. Some of these 'hotspot' loci include genes that regulate cell differentiation and growth factor signalling.

The increased methylation in these particular regions results in more highly condensed DNA, which greatly reduces the access of transcription factors that initiate the transcription of these genes. It's no wonder that as a result, the gene products (i.e. proteins produced from these genes that are involved in internal regulations) from these loci decreases greatly. For example, the increased methylation of SOD3 leads to misregulation of oxidative stress, which could induce oxidative damage to the eyes.

Other genes, such as MARK2 (which is vital in maintaining the movement of mitochondria in the retina and helps in proper neuronal function) and SP1 (which is crucial for corneal development) are also found hypermethylated, leading to increased refractive error and abnormal thinning of corneas due to a very low level of functional gene products. Additionally, based on investigations of children under the age of 12, other genes associated with myopia have been shown to have a CpG site with a reduction in methylation among myopic children. For example, the decrease in methylation on the CpG island of one of the semaphorin genes causes an elevated level of expression of SEMA5A, which has been significantly associated with myopia by inhibiting axon growth by retinal ganglion cells. This means that the length of neuronal fibres is reduced, inhibiting the retinal growth cones even in the presence of growth signalling molecules.

Furthermore, previous studies identified that genes related to myopia could also be found in the brain, affecting neuronal development and signalling. It is possible that myopia is initiated by a signalling cascade involving the sensory retina, choroid, and retinal pigment epithelium that results in changes in scleral physiology, such as elongation of the eyeball.

It is therefore important to limit myopia progression by reducing gaps in our knowledge on the condition, and collecting data on both

genetic and epigenetic risk factors. Hopefully, more research will be carried out to investigate the link between epigenetics and myopia, which may provide more information for the medical and public health sectors in early detection and therapeutic interventions.

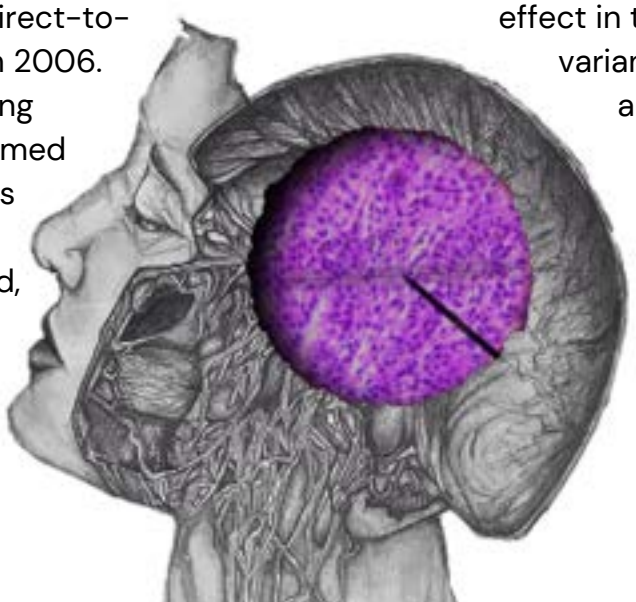
Kate Hodgson

Personal Genomics: Facts or Fad?

How much can personal genomics companies tell you about your health?

DNA: It is what makes you, you! Variations in our DNA sequences drive diversity amongst the human species. Geneticists work to discover which genetic variants connect to particular observable characteristics, focusing on variants linked to health conditions and diseases. Have you ever wondered what your unique DNA sequence can tell you? Personal genomics companies such as 23andMe allow consumers to have their DNA sequenced and analysed for variations associated with traits or conditions by simply sending in a saliva sample. These traits can vary from the trivial, such as your likelihood of disliking cilantro, to the more consequential, such as those associated with cancer development.

According to the National Human Genome Research Institute, the cost to sequence the entire human genome has decreased exponentially over the past two decades, from $100 million in 2001 to approximately $1000 in 2022. This decrease in cost coincides with the emergence of revolutionary sequencing technologies. Next-generation sequencing was introduced for commercial use in 2005, enabling the sequencing of multiple DNA strands simultaneously which made DNA sequencing faster and more efficient compared with its predecessor, Sanger sequencing. With a quicker and more accessible way to sequence DNA, 23andMe pioneered direct-to-consumer genome testing in 2006. 23andMe launched by offering an ancestry service that claimed to show the locational origins of the consumer's DNA. A subsequent service emerged, capable of informing consumers about their predisposition for health-associated traits.

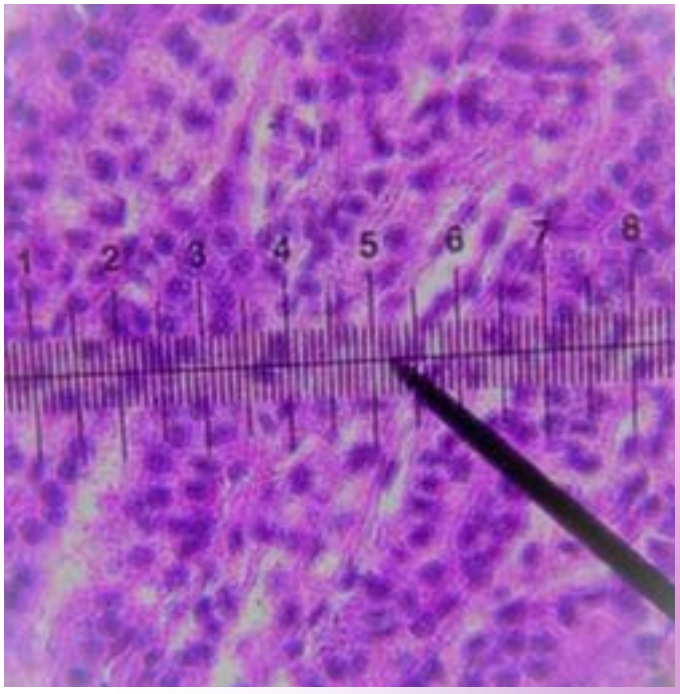


Since its beginnings in 2006, 23andMe has sold an immense 12 million DNA kits, demonstrating the popularity of direct-to-consumer genome testing with the general public. In theory, test results from these personal genomics companies could help people prepare for their future by providing knowledge about variations in their DNA sequence that could influence their health. Sounds promising, right? The reality is that there are many problems with this kind of personal DNA testing, particularly in how the sequencing data is analysed and correlated to the traits of interest.

A common kind of genetic variant sought out by personal genomics companies is called single nucleotide polymorphisms (SNPs). SNPs are locations at which single bases in the genome vary between individuals, resulting in different versions of the same gene. Genome-wide association studies (GWAS) are a method used to correlate SNPs with particular traits. This method compares the entire genome sequences of people affected and unaffected by a trait of interest and searches for the more abundant SNPs in affected individuals. GWAS, however, is not a flawless investigative tool. A major pitfall of GWAS is that it might detect variations that only have minimal effects on the trait when acting alone and instead have an additive effect in tandem with many other variants. Moreover, as GWAS is a correlational method, it is limited by the number and range of subjects used. Rarer variants associated with a trait will need a substantial number of study candidates to be detected.

In addition to the issues with variant-trait association methods, the search for trait-associated variants in the consumer's genome by personal genomics companies is, at best, superficial. Take the example of hereditary prostate cancer. 23andMe claims to estimate the relative risk of developing the disease but only searches for one variant in one gene correlated to an increased risk of prostate cancer. The target in question is the G84E variant in the HOXB13 gene. Nonetheless, the development of prostate cancer has been linked to more than 150 SNPs, and these variants extend beyond just the HOXB13 gene. The G84E variant is also only typically found in people of European descent, so the relevance of a negative test result to somebody of non-European descent is negligible. It is an oversimplification to base the risk of developing conditions as complex as prostate cancer by searching for a singular variant when many more are implicated.

Consumers of personal genomics tests should exercise caution when interpreting their results, especially those indicating potential health risks. The complexity of personal genomics, particularly the intricate impact of genetic variations on observable traits, underscores the need for careful consideration. Importantly, the data analysis methods employed to correlate these variants with traits, as well as the techniques utilised to forecast the risk of developing health conditions or diseases, are fraught with oversimplifications. The Food and Drug Administration substantiates this caution, advising that "results obtained from the tests should not be used for diagnosis or to inform treatment decisions."



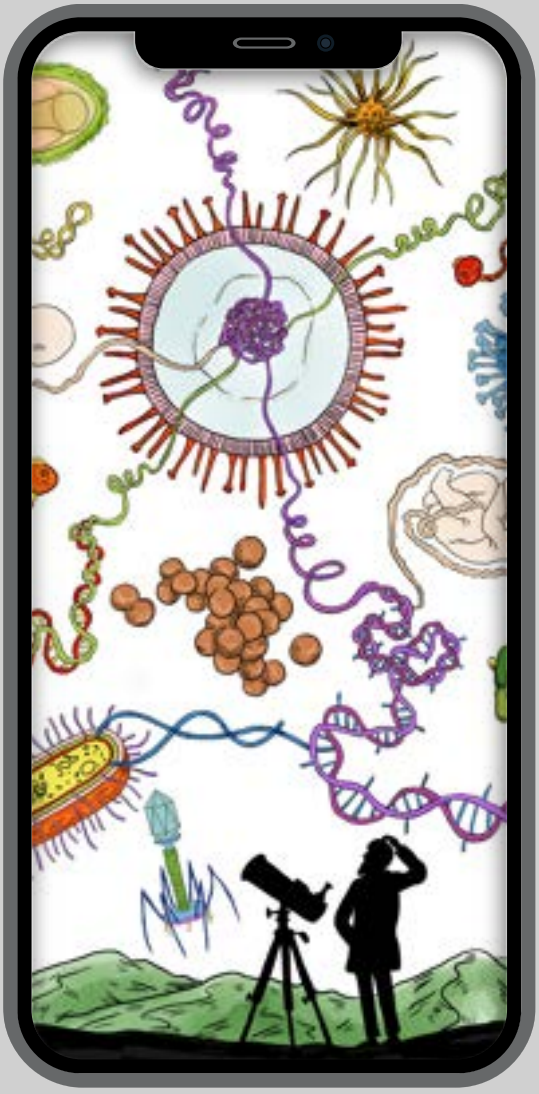
Illustrated by Bella Marwick

Evolving with Viruses

How Virolution Shaped and Saved Life on Earth

Emily Yang

While viruses have long been cast as the 'villains' of the biological world, the real story reveals a surprising twist. Unveil the hidden power of evolution and survival – viruses. Their pivotal role has shaped life on Earth and will continue to aid in the survival of living organisms, including humans.



Illustrated by Emily Yang

'Virolution' means virus driven evolution, a term coined by the author Frank Ryan in his book 'Virolution: The most important evolutionary book since Dawkins' Selfish Gene'. The theory presents a virus-centered view of life, suggesting that viruses are not solely agents of disease, but have always been key drivers of evolutionary change, much like other well-known mechanisms such as natural selection and genetic mutation. It has been found that viruses have a fundamental role in the development of life forms as well as the survival of the human race. Virolution involves the concept of a 'virolutionary arms race' in which viruses and hosts influence one another's evolution, necessitating continual adaptation. This has led to the evolution of various defence mechanisms in living organisms.

Viral elements constitute over 43% of the human genome, far exceeding the 1.5% attributed to the vertebrate component - the very essence of what makes us human. Viruses have significantly reconstructed the human genome by repeatedly integrating their genes into our DNA via symbiogenesis. This process starts with the virus colonising the human genome via infection from a closely related species, such as with the example of the simian version of the HIV that came from chimpanzees and mangabey monkeys. What follows is aggressive symbiosis, during which viruses challenge human survival through the course of epidermis and pandemics, ultimately leading to a profound transformation of the human genome.

The best explanation of aggressive symbiosis comes from the example of the relationship between virus and bacteria. Inside a bacterium, a virus deposits a copy of its genome that codes for two products: a long-lasting toxin and a short-lived antidote that protects the bacterium from the toxin's effects. From the bacterium's perspective, it appears advantageous to rid itself of the virus. However, when the bacterium attempts to eliminate viral entities, the anti-toxin effects wear off, while the persistent toxin continues to operate. Paradoxically, this viral strategy kills all bacteria that do not possess the virus themselves.

This initial appearance of aggression and selfishness ultimately transforms into a mutualistic relationship. Bacteria containing the protective virus become resistant to infections by other related viruses, including endogenous retroviruses. The newfound partnership sets the stage for the host's population to re-expands while co-evolving alongside the virus. The consequence is a reproductive separation between bacteria with the virus and those without. This process highlights the pivotal role of viruses in propelling the forces of evolution.

Aggressive symbiosis can give rise to a different phenomenon known as 'plague culling'. In this phase, viruses serve as covert allies to their hosts, infiltrating and attacking organisms lacking the protective viral shield. A notable example is the conflict between indigenous British red squirrels and imported grey squirrels from America. Grey squirrels carry squirrel pox virus, which, although harmless to them, proves fatal to the red squirrels. Here, the virus strategically aids the grey squirrels by eradicating their competitor.

The colonisation of the human genome has yielded profound benefits for our survival, becoming an evolutionary driving force. Viral genes play crucial roles in regulating the production of keratin, hormones, enzymes and even contribute to the development of essential structures like the placenta and immune system. These viral components are also expressed in various vital organs, including adrenals, testes and the brain. However, the improper sequencing of these viral genes by human's transcriptional machinery can also lead to disorders such as multiple sclerosis, haemophilia and cancer, which shows how important the role of viruses has played in our development. The colonisation of the human genome by viruses is an ongoing process and as time progresses, the viral proportion of our genome is expected to increase, ensuring that viruses continue to shape and influence the evolution of the human species.

Virolution is a truly groundbreaking concept that presents a compelling argument for the central role that viruses have played in the evolutionary history of life. Further research is required for a deeper understanding of the virolutionary processes which can have implications for medicine, genetics, and evolutionary biology, and lead to new insights into disease prevention and treatment.

Nature's Cushions

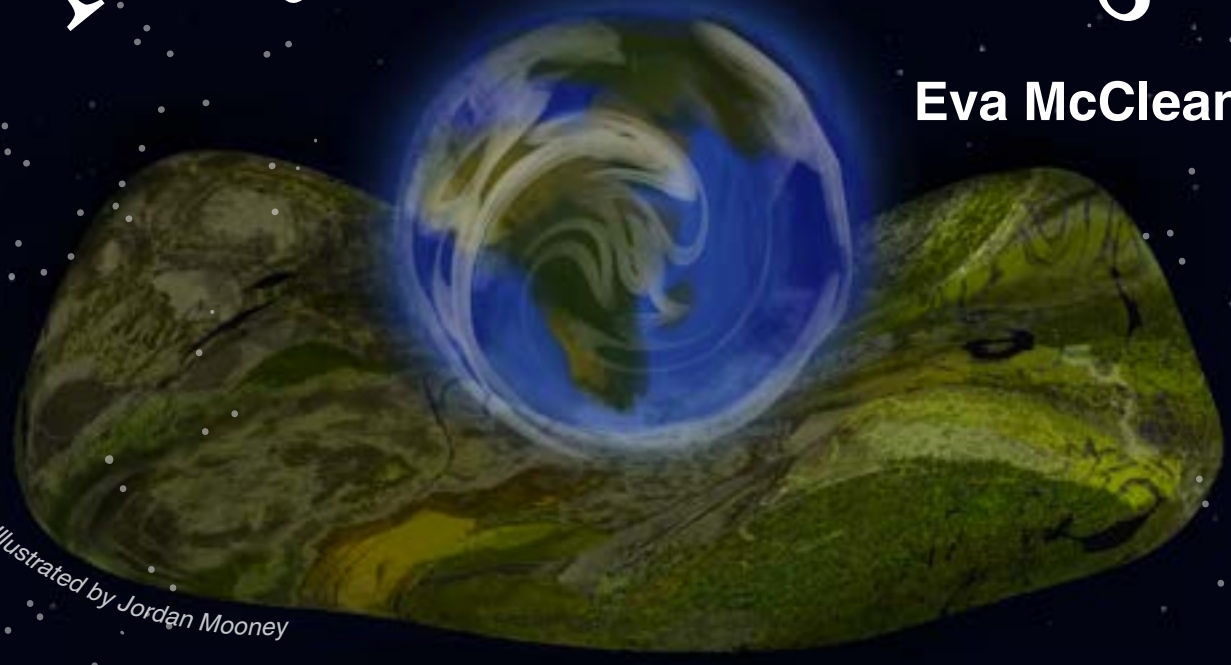
Our Forgotten Climate Saviour

Eva McClean

Hidden in the shady forest undergrowth, beneath the great towering oaks lies a detail forgotten by the busyness of today. Moss–simple by nature yet bursting with flourishing life amongst its own mini-forest ecosystem. This bryophyte has been cushioning our forest floors for 450 million years, long before human footprints were around to flatten their tiny leaves. Moss is non-vascular and absorbs all it needs from its surroundings by diffusion while being anchored to the soil by root-like rhizoids. Moss' leafy stem comprises the gametophyte, which is the haploid form, and when the moss undergoes fertilisation, a sporophyte is formed. This structure acts as tall stalks that expel spores, allowing them to take their gentle journey through the wind to their new home. Water controls the force of life through the mini green leaves, and they can't seem to get enough of it: some moss varieties can hold up to 5000% of their dry weight.

However, don't be fooled by this overarching dependence on water–moss can stay dry and dormant for many years without even a drop of its liquid life force.

Moss is a modest member of the forest community, speaking its wishes softly under the green leafy stems above it. This plant holds a diverse ecosystem of microfauna in its mossy hands. Tardigrades (warmly known as 'water bears'), nematodes, ciliates, bacteria, and fungi can be found roaming the tiny stems. Moss has a deep, loving relationship with the soil, influencing the microclimate by controlling temperature and humidity. Moss also has a highly diverse range of bacteria with many important functions, from nitrogen fixation to soil health maintenance and decomposition. One study found that biocrusts covered by moss in Southern China were positively affecting the soil nutrient and bacteria levels. Moss is beneficial in various habitats, from the boglands of rural Ireland to the stretch of your front lawn.



Illustrated by Jordan Mooney

Illustrated by Yasmin Yong

Moss is a pioneer species, meaning that it is the first to colonise new or disturbed habitats. It functions by weathering the area and then producing organic material that allows the land to be more hospitable to other species.

This is especially important in the context of climate change, as more and more areas are being degraded by anthropogenic causes. Their rhizoids allow them to anchor to a wide range of surfaces, unlike roots which need deeper, richer soil. Moss is well-adapted to living in shady, moist areas, hence why we can often find their resilient little stems persevering between cracks in our concrete-laden cities. However, moss can be very susceptible to the effects of pollution, as it absorbs everything from the surroundings by diffusion, be it nutrients or harmful pollutants. Therefore, in today's changing climate, moss is certainly under pressure.

The words 'climate change' loom over our heads like thunderstorm clouds and wait beneath our feet in swathes of quicksand. However, we must consider the solutions and take steps that lead to change, whether big or small. A crucial element of combating global warming and increasing biodiversity is persevering and restoring our precious natural habitats–one of these being boglands. Boglands are areas of decaying plant matter contained in a kind of marshy, freshwater soup. They are made of Sphagnum moss, which has incredible water-absorbing abilities that cause the bog to become waterlogged and anaerobic. This allows the partially decaying plant matter to be preserved and form peat–a fossil fuel. These boglands are a major carbon sink, and the destruction of these lands is detrimental to the climate. Bogs contain a third of all soil carbon, which is double the carbon that forests store. Clearly, bogs are not getting the love they should be! Unfortunately, large amounts of peat are being removed from the boglands, destroying habitats that took thousands of years to form and releasing CO2 in the process. Thankfully, there are some bog restoration projects underway, however, more needs to be done to preserve these ancient habitats and the delicate moss which supports them.

Moss may not always be at the top of our minds, but it will always be there beneath our feet in solace, helping the ecosystem which it surrounds. This bryophyte has been taking care of our earth for millions of years, and so its resilience may stand the test of climate change. From its bog-forming abilities to its diverse microfauna collection–moss has a trick for us all. No matter what happens, there will always be a mossy green cushion for you to fall back on!

In early September, I found myself looking into a glass cabinet at Croatia's modest Natural History Museum in Split. I noticed these Frankenstein-like structures of shells adorned with bits of coral, rocks, smaller shells, and sometimes even shark teeth or sea glass, as if they had been superglued together. But instead of being the work of an eccentric museum curator, they were built by the creatures themselves.

These specimens were shells from the Xenophora; a genus of snails that collage themselves by adding things to their own shells. Objects are chosen and positioned using their proboscis, a long, extendable tube with a harpoon-like tooth at the tip. Then, a special glue made of calcium carbonate is secreted from their mantle, the organ that forms the outer wall of the snail's body and builds up their shell. This crystallises and hardens, permanently sticking the object to its shell. Each snail is unique, forming beautiful, complex structures; sometimes they assemble uniform radiating patterns on their shells, whilst others appear more irregular and chaotic. The protrusions function as armour, defending and camouflaging them from predators. For snails inhabiting deeper waters, their increased surface area helps prevent them from sinking into the soft floor.

Despite their beauty, Xenophora clearly aren't acting out of a profound appreciation for the visual arts; this behaviour is practical, providing evolutionary advantages to them.

I began to question whether animals exist that do have an appreciation for aesthetics. As I delved deeper I found numerous examples of animals decorating themselves, from caddisfly larvae forming ornate cases to pupate in, to decorator crabs camouflaging themselves with different objects. But it was the ones that appeared to have no increased fitness associated with such behaviours that struck me the most.

Aesth

Illustrated by Macarena Undurraga

Male bowerbirds build structures called bowers, made of thatched sticks and decorated with colourful objects, as part of their mating ritual. Females choose a mate based on the appearance of his bower. Each bower is unique; a study from 1985 showed that when provided poker chips of different colours as decorations, there were distinct preferences for certain colours between individuals. Furthermore, the birds positioned the poker chips in a very intentional way, grouping colours together, and sometimes even changing their minds and reorganising.

IN THE ANIM

The researcher John Endler puts forward that bowerbirds have an aesthetic sense and create art, as the structures serve no clear purpose, and this sense is required for building and judging them.

...etics

...AL KINGDOM

Amber Stratton

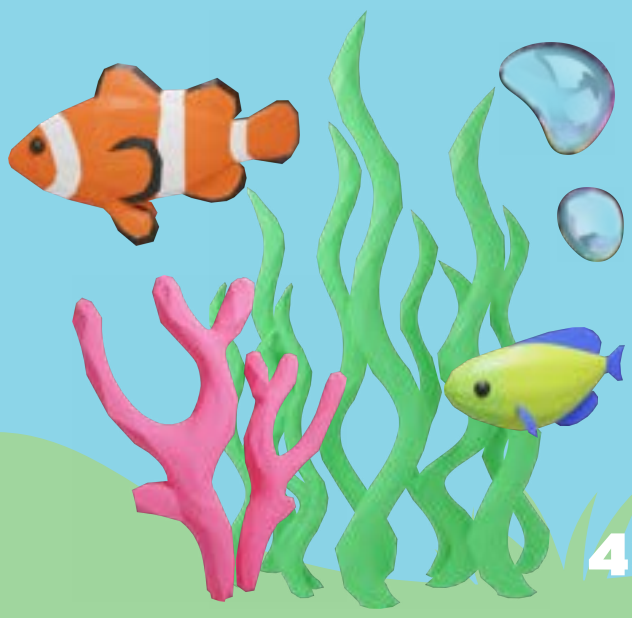
Many animals exhibit behaviours which could be interpreted as 'fashion trends'; in 1987, there were sightings of orcas wearing dead salmon on their heads. One female was observed starting this trend, which was then copied by others in her pod during a 5 to 6 week period.

After this, there were no more sightings of orcas with salmon hats. Again, this behaviour seemed to have no practical benefits.

Similarly, in a Zambian chimpanzee orphanage in 2010, a chimpanzee named Julie was seen picking blades of glass and sticking them in her ear. Over the course of a year, other members of the group copied this behaviour, continuing even after Julie, the inventor of this trend, had died. Researchers believed there to be no adaptive value to this 'grass in ear' behaviour and that it started from Julie simply showing playful behaviour and decorating herself. They argued that it points towards a level of culture being developed, which agrees with the orca study authors, who hypothesised a level of culture found in great apes and cetaceans.

We are just beginning to understand animal behaviour, and we've been proven to have grossly underestimated their intelligence and capabilities in the past. Often, we find ourselves judging their intelligence and capabilities by our own human standards, such as training pigeons to distinguish between Monet and Picasso paintings or teaching animals in captivity to paint under human instruction.

Whilst we must tread carefully when applying human ideas to animal behaviour, I think it's difficult to deny that these observations point towards a level of appreciation for aesthetics within the animal kingdom. Bowerbirds must appreciate the beauty of their bowers to have individual preferences in either building or choosing them. Orcas and apes are known to be thoughtful, intelligent animals, often engaging in playful behaviours, so perhaps it isn't a huge leap to suggest self-expression through aesthetics could be an extension of this behaviour. Moving forward, I think it's particularly important to avoid judging animal intelligence and behaviour by how well it mirrors ours, and rather study species in their own complexity.



Suzie Mishima

Microgravity in Biotechnology

Have you ever wondered what goes on up in the International Space Station? The ISS National Lab, a remarkable scientific outpost since its inception, has served as a vibrant centre for advancing the field of biotechnology for almost 20 years. What sets it apart as arguably the most unique laboratory in the universe is one distinct attribute - microgravity.

Microgravity is a near -zero gravity environment, which, simply put, is the sense of weightlessness that an astronaut would experience in space. This results from the constant freefall of the ISS in Earth's orbit whereby the speed of orbit is so fast that all masses in this orbit are constantly falling. In microgravity, traditional rules governing physical processes on Earth no longer apply. Gravity is a force that we take for granted and without it, fundamental biological processes behave differently.

Tissue Engineering

Even within our bodies, the effects of microgravity wield considerable influence on our health, triggering the degradation of muscle, bone, and cartilage. These physiological changes present formidable challenges to the prospects of space exploration, prompting dedicated research to combat these issues. Tissue engineering and regenerative research under microgravity has been an exciting opportunity into understanding how these conditions can be treated, since for example, cartilage tissue has limited regenerative potential. Some studies suggest that stem cell derived cartilage tissue growing under microgravity conditions display remarkable capabilities in proliferation, differentiation, and the overall production of superior quality tissue. At this intersection of space science and regenerative medicine, these breakthroughs raise optimism for the potential use of artificially grown cartilage tissues in microgravity as viable replacements for deteriorated cartilage.

Illustrated by Shangyu Chen

Protein Crystals

Microgravity has also been instrumental in the field of drug discovery by reimagining approaches to the tried-and- true technique of X-ray crystallography. This may sound familiar as it was the key to discovering the structure of DNA back in 1952, and is still used to this day in revealing the structures of proteins for drug development. X-ray crystallography reveals a molecule's 3D shape by concentrating X-rays on a crystalized sample of the molecule, which, after mathematical analysis, reveals the precise arrangement of its atoms. Despite being anestablished technique there are inherent limitations that deem certain protein structures to be 'unsolvable.' Gravity is one of the culprits as it creates convection currents as the protein molecules interact with each other during crystallisation, which results in defective crystals. Enter microgravity—here, the absence of these disruptive currents allow protein molecules to randomly arrange themselves, fostering the creation of more organised, high-quality crystal structures.

A drug to combat Duchenne Muscular Dystrophy (DMD), a severe disease of muscle degeneration, has been developed based on a protein crystal revealed aboard the ISS. Phase 3 trials are currently underway, with the hope that the drug, TAS-205, could double the lifespan of DMD patients. Other projects aiming to decipher the specificities of drug targets. such as the elusive breast cancer Bax inhibitor-1, hope to develop better treatments.

Drug delivery

Once a drug has been developed, a critical challenge emerges: - how to effectively deliver a drug to maximise efficacy. In 2019, Aphios Corporations secured access to the ISS to pioneer the development of drug-encapsulating particles on the pico-scale. These 'picoparticles' were designed to deliver a leading Alzheimer's drug candidate known as Bryostatin-1 to the brain. Through microgravity, they were able to reduce the size of a typical nanoparticle from 88 nm to less than 3 nm. A smaller particle is desirable as it can penetrate the blood brain barrier, as well as reduce dose per treatment due to high surface area to volume ratio. Aphios' ambitious objective is large-scale manufacturing of these picoparticles to treat Alzheimer's, all while curbing costs per dose through microgravity technology.

Future in Microgravity Research

Last year, NASA unveiled the decision to decommission the International Space Station (ISS) in 2031, marking a pivotal moment in space exploration. Does this mean the end of microgravity research? The growing commercialisation of space suggests otherwise as private companies, including Elon Musk's SpaceX, are set to replace the ISS. Although microgravity research is still in its early days, the demonstrated potential of the ISS has generated unprecedented interest in microgravity in this new frontier of biotechnology.

UNRAVELLING PURPOSE:
TELEONOMY IN EVOLUTION AND IMPLICATIONS FOR AI

Caleb Scutt

Despite their intrinsic interrelation, the connectedness between evolution and philosophy is often shunned in scientific discourse. Centuries of religious dogma and historical division between the realms of science and philosophy have exacerbated this schism, leaving academics treading warily when commenting on these matters. A particularly interesting topic, and one that has been the subject of revived attention recently, is the concept of teleonomy. Teleonomy is derived from the idea of teleology, which is the notion that things happen in an attempt to achieve a certain goal. It is best described by the French biochemist Jacques Monod, who defines teleonomy as 'the quality of apparent purposefulness and of goal-directedness of structures and functions in living organisms brought about by natural processes like natural selection.' The key distinction is that teleonomy only describes something that appears as purposefulness, rather than an action that is intrinsically goal-oriented.

The current state of evolutionary theory as we know it is absent of purpose; conventional schools of thought consider evolution a result of stochastic mutations and natural selection. When considering that an upper limit of 15% of our genome is functional, the remaining portion consisting of remnants of our ancestral genetic history, clearly any directional purpose that evolutionary forces are under is weak, or potentially non-existent. However, we see goal-motivated actions in almost every aspect of biology. From the smallest of cells right up to entire ecosystems, the natural world is built of blocks within frameworks that each serve their... purpose.

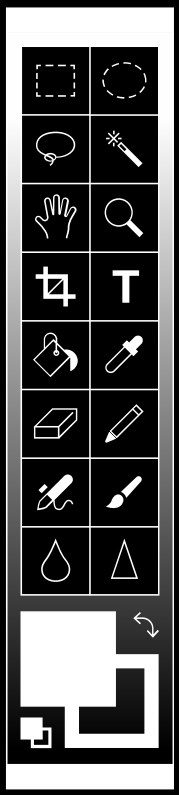
It is therefore undeniable that we all have an 'internal teleonomy,' which calls into question what we think we know about evolutionary theory and has wider implications in fields such as AI ethics.

It is easy for the debate around teleonomy to wade into precarious waters when ideas such as intelligent design and the anthropic principle are thrown into the mix, and evolutionary theory rejects any influence of outside purposes. How then do we explain the innate behaviours and processes exhibited by organisms all around us? Does a turtle come ashore and lay its eggs, or does it come ashore to lay its eggs?

Illustrated by Fion Lam

Ernst Mayr, one of the most renowned evolutionary biologists of the 20th century, commented extensively on the debate of purpose in evolution. Mayr suggested that the apparent purposefulness in organisms is 'on the basis of a program' and 'a code of information.' Only now, in recent advances in research, are we understanding the complex nature of inheritance that explains this 'purposive behaviour.' Phenomena such as sexual selection, epigenetics and reciprocal causation all stimulate purpose within an organism and are part of this internal teleonomy written into our genetic code. A key example of this is the phenomena of maternal effects, whereby mothers are able to influence the evolutionary trajectory of their offspring by epigenetic mechanisms. Traditional Darwinists would argue that this action is for the benefit of the offspring and thus is congruent with the theory of natural selection. Yet altruism within the natural world challenges this concept and hints at a collective and higher-level purpose that supersedes individual survival. This is not limited to organisms with consciousness; deviations from homeostasis and subsequent mechanisms to restore stability and reproduce are all goal-oriented actions in an organism. Throughout the natural world, it is easy to observe organisms driving their own evolution by programming written in their DNA.

Considering organisms from this reductionist viewpoint has significant implications as we head into the age of AI. While evolutionary theory has the potential to inspire and stimulate AI research using genetic and neural-inspired algorithms, the philosophical issues Mayr's concept of teleonomy presents leave us with more questions than answers. Such reductionism makes it difficult to find the distinction between the genetic code of living organisms and the computer algorithms of AI. We are left with a deterministic outlook that devalues the complexity of living systems and undermines our own autonomy. The ethical implications of this regarding AI are dangerous. Recent evolutionary synthesis reveals that organisms are more in control of their own evolution than previously thought. If the direction and purpose of our own evolution can be driven by our own genetic code, does this not apply to AI as well? Rather than ostracising those for debating these important questions, it is important that scientific discourse continues to wrestle with the concept of teleonomy and its role in evolution. Coming to terms with our own purpose, or lack thereof, is crucial before we venture too far down the path of AI.



WHY THESE STRIKES MATTER!

Altay Shaw

Our Medical Students need to be heard before we reach the point of no return.

The 6th October marked the end of the latest period of strikes for junior doctors and specialists across the country. The mandate, which was approved on the 31st August, states the BMA's full intentions of reaching full pay restoration and improved working conditions of all junior doctors in the UK. These strikes have not only brought to light the conditions doctors are being forced into but also cover the issues that the current final year medical students face.

Why are Junior Doctors Striking across the United Kingdom?

Since 2009, the real term pay of doctors across the United Kingdom has fallen by 26.1%, despite previous efforts by the British Medical Association (BMA) to increase total investment in 2019. The starting salary of £32,398 may seem reasonable, but after accruing debts across a minimum of 5 years at university, more than 50% of junior doctors were struggling to pay their utility bills.

Whilst media outlets will suggest that the ultimate cause of the strikes is pay, several reasons exist for the strike action. For example, there are currently over 10,000 vacancies in secondary care within the NHS. This may seem relatively small when compared to the over 125,000 vacancies in Hospitals, but shortages within Nursing have a direct impact on the workload that doctors are expected to do. This has resulted in some departments across the NHS having close to 70% empty positions within their training schemes.

Adding to the severe understaffing within different departments, medical staff also face unacceptable working conditions. Many doctors are unable to take lunch breaks, in part because some staff do not get time scheduled for breaks within their working hours. Numerous doctors state they do not have access to either catering or rest facilities when their contracts ask them to work out of hours. This is critical to highlight as the 2016 doctors' contract made working weekends and night shifts part of the contract, where previously they had been separate from the main working hours. These conditions make working within the NHS as a junior doctor unhealthy, and at times, dangerous as suicides have been attributed to overwork.

How are the strikes impacting medical students?

The cost of living crisis has not solely impacted the livelihoods of doctors. Medical students across the country continue to watch the outcome of the strikes as their financial burden to complete their studies increases. A study carried out by the BMA in Scotland found that 73% of medical students surveyed stated studying at medical school had severely impacted their finances. Unlike other university courses, students are set to a high expectation of attending a full day at clinics and completing self study outside of normal hours. The physical demands can prevent students from holding part-time employment as students may spend a minimum of 40 hours per week on the wards.

On top of the workload, during the strike period in March of this year, medical students were being urged to cover for striking doctors. This was not solely limited to a few hospitals across the country; medical students here at UCL were asked to cover both during the nursing strikes and doctors' strikes by hospital management in an attempt to reduce the strikes' impact. Many doctors condemned these actions, stating that medical students have not received the necessary training or carry the necessary indemnity cover to protect them in the event a patient were to pass in their care.

It should also be noted that medical students are not allowed to attend strikes or join picket lines. Although visiting the picket lines, creating signs, and sharing posts is allowed, many medical students are actively discouraged from engaging in the strike action. The BMA has stated that students should continue to attend their placements as directed by their medical schools, and little protection is offered to students who go in during strike days. UCL still holds the line of wanting students to attend during the strikes, despite these practices having affected many on their placements.

Illustrated by Jordan Mooney

Where do we go next?

With the announcement of the government's plans to extend new strike laws to medical professionals across the country, it will become harder for the same number of doctors to take part in industrial action. Minimum service levels will aim to have a cover of care to "protect patient safety" when industrial action is called. As previously discussed, there are shortages across multiple trusts and departments, meaning most wards are already understaffed, causing great stress to those working in unaffected periods of time.

What the strikes have successfully done is demonstrate that the issues being faced by the junior doctors are also quintessential to the future of medical students across the country. As we face a potential exodus of doctors to other countries or out of medicine completely, the strikes have brought the struggles that are being faced by medical professionals to the public's attention.

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