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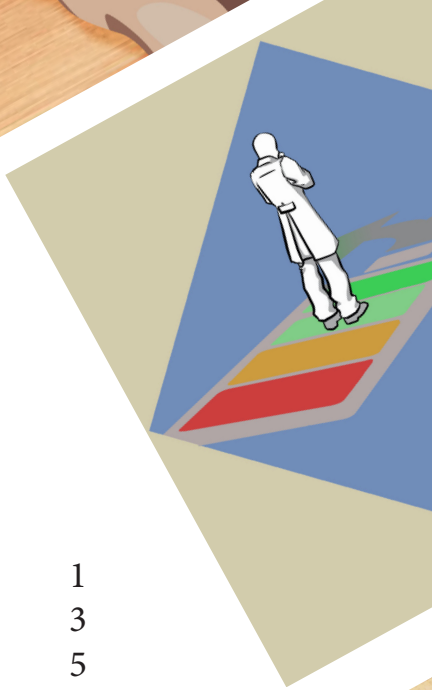

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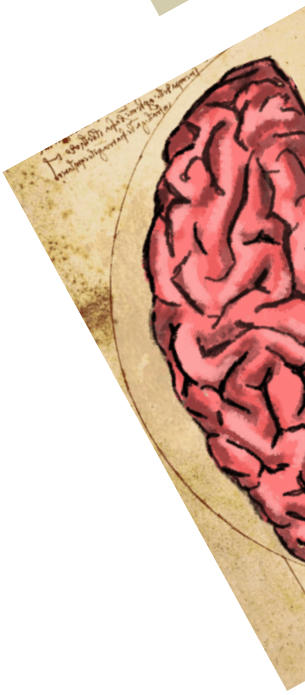

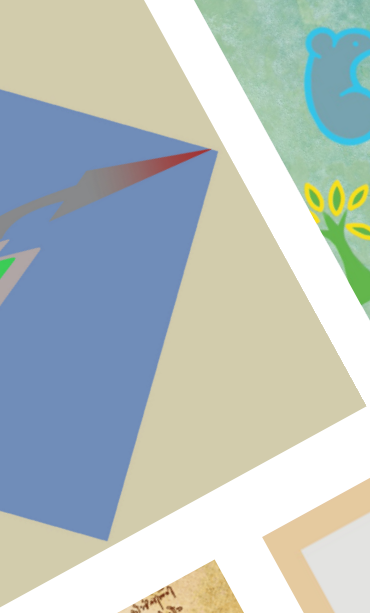


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COVID-19 and the brain; A new wave of neurological disorders

Memory problems, chronic fatigue, psychiatric illness: How COVID-19 can cause extensive damage to the brain

Written by Clíona Farrell

COVID-19 has paralysed the world for more than a year. Although we know COVID-19 as a respiratory illness, the profound effects it can have on the brain are astonishing. In a recent panel at the virtual Cold Spring Harbour Neurodegenerative Disease Conference, prominent neurologists Dr. Walter Koroshetz and Dr. Anna Nordvig gathered to discuss how COVID-19 can cause extensive damage to the brain. The audience, including myself, was struck by the sheer number of neurological symptoms now known to be directly associated with COVID-19. From chronic fatigue to stoke, psychosis to anaesthesia resistance, the possible consequences seemed endless.

During COVID-19 infection, the most common symptoms that affect the nervous system are muscular pains, headache, fatigue and loss of taste and smell. But patients can also develop strokes, delirium, encephalopathy and brain swelling. Generally speaking, patients with more severe respiratory infection can develop more debilitating neurological symptoms. However, in July 2020, a study from the UCL Queen Square National Hospital for Neurology showed that this is not always the case. In their study, some patients with severe neurological complications, including neuroinflammatory disorders and stroke, had not suffered severe respiratory COVID-19 disease.

Because people infected with SARS-CoV-2 can lose their sense of taste and smell, it was initially proposed that the nasal passages might offer a route for the virus to attack the brain. Instead, scientists showed that the virus infects not the neurons themselves, but epithelial cells that line the nasal passage. These cells support the olfactory neurons and when they are not functioning properly, our sense of smell and taste can be disrupted.
Not only are people suffering from neurological complications during COVID-19 infection, but post-infectious disorders such as 'brain fog' have been widely reported. Today, thousands of COVID-19 survivors are suffering from debilitating neurological conditions months after initially testing positive. Post-COVID brain fog covers a wide range of symptoms and affects people in many different ways, with sufferers describing memory problems, fatigue and even new anxiety and depression after recovering from the initial infection. In a survey characterising long COVID in more than 3,500 international patients over a 7-month period, the most common persisting symptoms were fatigue, cognitive dysfunction and post-exertional malaise, each affecting between 50-80% of the cohort. It is currently unclear how long these effects may last.

But how exactly is SARS-CoV-2 causing neurological complications? In healthy individuals, the brain is protected from the entry of unwanted or toxic materials, including viruses, by the blood brain barrier. Early in the coronavirus outbreak, the question on the mind of neuroscientists and neurologists alike was whether this virus could surpass or penetrate the barrier. By now, multiple autopsy studies have been conducted on the brains of people who have died from COVID-19. Although there is a mixed verdict among doctors, most studies have failed to show many, if any, virus particles inside the brain. When compared to Rabies, a virus that specifically acts to infect the brain of the host, the viral load within the brain of COVID-19 patients is minimal. But of course, we also have to remember that post-mortem studies only show what happens to the sickest patients, and not those who survive the infection.

If the virus cannot reach our brain, how is it causing such debilitating neurological deficits? The virus enters the body through the nose or mouth. From there, it moves down to the lungs, where it can enter our blood – a path to organs all over the body. On recognising the virus, the immune system reacts by sending a flood of immune cells and inflammatory molecules, called cytokines, to attack the virus. This attack can trigger an inflammatory reaction in the brain, where the resident brain immune cells, called microglia, release more inflammatory cytokines and free radicals.

Like in the nasal passage, the virus can also attack the epithelial support cells of the blood brain barrier, kicking the inflammatory state of the brain into overdrive. This cycle of inflammation can be further propagated by oxygen deprivation associated with COVID-19, even leading to blood clots and strokes in some patients. What starts out as a protective response to fight the virus can lead to chronic inflammation, harming neuronal cells. Depending on the function of these neurons, cognitive or motor circuits can be affected. This is seen in long COVID sufferers and is likely to contribute to many of the neurological symptoms caused by the disease.

As scary and strange as these neurological disorders may sound, pandemics of the past, including the 1918 flu pandemic, SARS and Ebola, have all been linked to nervous system complications, from neuropsychiatric disorders to Parkinsonism. After the original SARS outbreak, a follow up study in Hong Kong showed 40% of infected patients suffered from a new psychiatric illness and/ or chronic fatigue months after recovering from their respiratory infection, likely caused by a similar neuroinflammatory reaction as in COVID-19. These disorders prevent people from returning to their lifestyle prior to infection; some people can no longer work and others suffer from strained personal relationships. It is still early days for long-term COVID-19 research but these insights from previous pandemics shine a light on the possible health consequences for sufferers of COVID-19 that may last a great deal longer than the infection itself.

Neurological effects of COVID-19 can be temporary or more long-term, particularly in those who suffer from severe infection. However, it's not just the elderly who are at risk. People in their twenties, thirties and forties who have never had psychological problems or sleep disturbance before are also presenting with these symptoms. The good news is that clearer research on these questions is emerging each day. With the number of vaccines being produced and administered increasing, the prospect of stopping the spread of COVID-19 and its associated neurological deficits is within reach. Here in the UK, as we follow the roadmap into a post-COVID world, hopefully understanding these risks makes it that small bit easier to stay sensible until it is safe to emerge in summer 2021.

Art by Doheon Kim

Is science neglecting PTSD patients?

NICE does not recommend a new nasal antidepressant. What does this mean for patients?

Written by Viktorija Vaitkeviciute and Eugenia Wong

Post-traumatic stress disorder (PTSD) is a disabling condition, resulting in grave consequences if not treated properly. It is the fourth most prevalent psychiatric disorder in the US and around 8% of the global population will receive a diagnosis in their lifetime. The current treatments for PTSD are limited and there is an imperative need for further research. Well-known psychiatric disorders, such as anxiety and depression, seem to attract more attention compared to PTSD. Additionally, as a fallout of the current pandemic, we may see an increase in PTSD cases. It is therefore essential to ask whether enough is being done to tackle this pressing issue and provide support for its victims.

PTSD: what is it?

PTSD is a debilitating psychiatric condition, induced by physical, sexual, or psychological trauma. To be diagnosed with PTSD, an individual should have the following symptoms: avoidance of thoughts and reminders about the trauma, intrusive trauma memories, negative mood and cognition, as well as general hyperarousal (irritability, insomnia, poor concentration).

The main pathophysiological features of PTSD are fear dysregulation and the impairment of brain-mediated fear responses. The easiest way to explain this is through Pavlovian fear conditioning, which is used to study PTSD. The subject is initially given a neutral conditioned stimulus (light, tone, image, etc.), paired with an unconditioned one (shock). A conditioned response forms when the two stimuli are associated: a subject starts having a fear response after the neutral signal as they are expecting the shock to follow it. Healthy people can halt their fear response once the threat is removed. Whereas, PTSD patients continue to feel fear.

Interestingly, stress during childhood can induce epigenetic changes that have an enduring effect on the stress response as an adult. FK506 binding protein 5 (FKBP5) blocks the binding of stress hormones to the glucocorticoid receptor. This binding is essential to induce the stress response and, subsequently, to switch it off. It has been reported that stress during childhood can result in long-lasting demethylation of the FKBP5 gene, which upregulates its expression and impairs stress responses in adulthood. Therefore, epigenetic studies can provide a better understanding of PTSD and help to predict which individuals are more likely to develop it after a trauma.

Current treatment

The current first line of treatment for PTSD is psychotherapy, both trauma-focused and non-trauma-focused. Trauma-focused interventions such as prolonged exposure therapy (PE) aim to abolish the patient's fear response to the traumatic memory. A study reported that 41-95% of PE participants were no longer diagnosed with PTSD at the end of their treatment. However, effectiveness is significantly limited by dropout rates, which range from 10-38% in randomised clinical trials — this figure is predicted to be higher in community settings. This is likely attributed to avoidance symptoms, which are closely associated with PTSD.

Pharmacological approaches for PTSD are even more limited in efficacy than psychological treatments. Currently, there are only two FDA-approved selective serotonin reuptake inhibitors (SSRIs) for PTSD (sertraline and paroxetine). SSRIs have been shown to relieve PTSD-associated symptoms such as re-experiencing, avoidance, and numbing. However, pharmacologic agents are not universally effective — less than 60% of patients respond to treatment in a clinically relevant manner and only 20-30% fully recover.

Issues with the current approach

With poor accessibility to treatments and ineffective interventions, it is unsurprising that PTSD patients often turn to substance misuse. Substance use disorders are highly comorbid with PTSD. A study examining the relationship between PTSD, childhood trauma and substance use found high rates of lifetime dependence on recreational drugs in the traumatised population: 39% alcohol, 34% cocaine, 6% opiates, and 45% cannabis. This creates an additional issue of drug addiction, which in itself is a major public health challenge and imposes a tremendous socioeconomic burden. Therefore, better, efficacious treatments must be made available to PTSD patients so that they aren't forced to self-medicate in dangerous ways.

The issues with current treatments involve not only limited options but also a lack of their utilisation. A study reported that only a minority of Iraq and Afghanistan veterans with PTSD completed the recommended mental health sessions offered by the US Department of Veteran Affairs within the first year of their diagnosis. Being less than 25 years old and male was shown to correlate with not completing treatment. This might be due to avoidance, comorbid depression, other priorities (school, employment) and the existing stigma for seeking help. Additionally, it was suggested that living far from treatment facilities also increased the likelihood of non-completion, which could be improved in the future.

Perhaps the key to helping PTSD patients does not just rest in treating them after the fact, but rather identifying and training at-risk individuals. For instance, deployment anxiety reduction training (DART) aims to increase an individual's resilience to a potentially traumatic stimulus. However, since trauma cannot be predicted in many cases, this is only possible for a subset of the population. Nevertheless, more robust measures need to be implemented to support patients to ensure they are not left out in the cold in the aftermath.

Tackling this disorder is becoming increasingly necessary as the ongoing pandemic might result in a surge of PTSD cases among healthcare workers and the general public. The current situation has significantly affected all of our mental health in ways we would have never thought it could. While 'self-care' is becoming a buzzword, just talking about it will not result in real, substantial solutions. Therefore, PTSD research focusing on improving treatment options is essential to provide adequate support for those in need.

Art by Grace Gu

Psychological decision making in the stock market

How should you think about stocks?

Written by Altay Shaw

The recent events that shook the stock market are still filling the headlines. GameStop, a Texas-based game retailer, was facing a 'shorting' by hedge fund managers. This is where a stock is undervalued so that individuals can profit in the short term rather than waiting to get longer-term dividend payouts or bonuses from a company. This attempt was thwarted by a subreddit group called r/wallstreetbets, that invested heavily and prevented the company from going into bankruptcy. Since the effort, proceeds of their work have gone to several charitable causes, including Gorilla Funds.

Though the events have brought into question the legality of hedge fund business practices, it does raise an important psychological point. Finances are almost constantly on our minds, so it is important to consider how decision making and analysis are shaped by neural wiring and social influence.

How does psychology apply to trading?

To understand the decisions made in trading, it is important to become acquainted with the term 'trading psychology'. When trying to succeed in the world of trades and shares, people will typically be overcome with a sense of avariciousness, a greed for gaining wealth. Novices and professionals alike are vulnerable to feelings of catastrophic loss when a trade goes wrong.

With this in mind, one may assume that the safest way to approach the stock market would be to take a calm and measured approach to trading. But, in most of the literature, the opposite is true. In studies that have been carried out into 'behavioural finance', there is an overwhelming consensus that individuals tend to play down their situation, claiming poor chance hampered them. This compromises their ability to judge risk, causing them to go beyond their limits, which is worsened when people put higher amounts into risky situations.

What form of decision making works best for the stock market?

On the stock market, you can have two different positions. A short-term position is where you stand to make money on a short-term purchase of shares for up to a year, whereas in a long-term position, you hope to make larger profit – provided that the buying power of the money invested either stays the same or increases above the rate of inflation.

As a result, the decision-making process can be separated into two parts. There's the split-second, in-the-moment decision to act fast to make a profit, which is wired within the cerebellum. The alternative is making a lengthy analysis of the past months of the stock and reading analysts reports about the future prospects of a company, which takes place in the frontal lobe.

The process itself is more complex than simple localisation. In a 2017 study published in Neuron, neural activity was mapped by functional MRI when long-term decision-making occurred. In the test subjects, habituation to experiences allowed the animals to associate actions with positive or negative outcomes. This was able to demonstrate that in addition to the cerebellum's well-established role in coordination and balance, it is also associated with control of emotions in reaching outcomes.

How do group decisions and precedents affect future situations?

Before the start of the year, many of us would not have considered ourselves to be financially literate. Maybe a parent or friend would mention a pension plan or their intent to invest but that would have been the extent of it. However, the political fallout following the decision of the trading app Robinhood to ban users from investing in GameStop, in order to protect hedge funds from losing large sums of money, has brought some questions to light.

The episode of events has offered an interesting outlook on how reaching an outcome can be affected when a collective comes together. This falls under the principle that group decision-making should allow for a greater

number of individuals to come together, considering different viewpoints and ideals in order to make the optimal choice for the group. These ideas were popularised in the late '70s, with Birt Duncan suggesting that a diverse group should be used to reach a decision, but a like-minded group is necessary to implement a change with minimal conflict.

The effort made by r/wallstreetbets could be seen under this light. Social media-fuelled hype over the stocks was essential to ensuring people were made aware of the situation. Researchers at Oxford University showed that with correct targeting and discussion, individuals were more likely to heed the advice given by members of the Reddit group and invest in the GameStop shares.

However, it is important to exercise caution in these matters. Whilst stocks can be a reasonable way to invest, getting sound advice is essential. r/wallstreetbets, though a group of like-minded individuals, is not accredited. Investments are volatile and though GameStop has worked for them, the saga of Hertz did not end so well despite efforts to increase the share price tenfold.

In addition to this, groups that are mobilised to target specific stocks can cause high fluctuations in value. This can lead to volatility and forced control by companies, including Robinhood, to protect their own interests.

Longer-term outcomes

We will have to wait for further updates in regards to the Robinhood case – what rules and restrictions will be put in place as a result of the final verdict. Any measures that arise will have a lasting impact, if not in the form of radical change but, in the approach to trading and whether non-finance workers, individuals wanting to make 'passive income', will be able to take advantage and gain by playing a long game.

The trading long game.

Art by Patrick Marenda

The tactility of digital texts

Electronic books are becoming more popular, but research suggests that reading on paper still boasts unique advantages.

Written by Anastasiya Kolesnichenko

Secondary-schoolers across the Scottish border live in the future. When they get ready for classes, they don't pack their backpacks with textbooks – they charge their iPads instead.

As participants of the Inspire Learning Programme, Scottish children are immersed in their gadgets during lessons. The devices were introduced in the classrooms to help learners develop technology skills and enhance their future employability.

The benefits of this new digital education strategy were plain to see during lockdown. Pupils and teachers who have used technology for study previously adjusted more easily to remote learning. While there are advantages to giving access to electronic books, are there shortcomings of taking paper books away from students?

In Scholastics' 2012 report, children said that eBooks were superior when they were travelling or did not want their friends knowing what they were reading, but preferred print books for sharing with friends and reading at bedtime. Additionally, participants of Naomi Baron's 2016 study praised digital reading for the ease of finding material, the ecological benefits and enhanced multitasking. However, a 2019 study from New Zealand found that participants tended to read more thoroughly when engaged with non-online content.

Understanding how reading on paper differs from reading on screens requires some explanation of how the brain interprets written language. Professor Maryanne Wolf of UCLA explained that people are not born with brain circuits dedicated to reading. Thus, when children learn to read, their brains regard letters as physical objects and improvise a new circuit for reading by weaving together various neural tissue regions devoted to other abilities, such as spoken language, motor coordination, and vision. After all, humans did not invent writing until around the fourth millennium B.C.

The ever-present issue of the potential death of physical books has been extensively studied for decades. In 1992, scientists hypothesised that people read slower and less comprehensively on screens than on paper. Since then, studies have proven this assumption wrong, yet the debate has persisted.

In 2013, Professor Anne Mangen of the University of Stavanger in Norway found that it was harder for students to quickly complete a short-answer quiz based on a text when they read it on a PDF than on paper. From the study, Mangen concluded that the difficulty was linked to a digital format's poor navigation. Students couldn't find necessary information efficiently in the text as they had to scroll through it one section at a time. Part of the navigation issue is connected to how people recall information within the text body. When trying to remember, people picture where in a book they read it.

In his book Book Was There: Reading in Electronic Times, Andrew Piper noted that humans need to know where they are in time and space. It is important that reading provides a similar sense of orientation that offers the chance to go back and evaluate one's understanding of a text. An open paperback presents the reader with enough information to orient themself: the left and right pages, a total of eight corners, margins, the thickness of one side of the book. Alternatively, the screen only displays a single virtual page. The length of a digital text is often represented with a scroll or progress bar. Some pagination is preserved: pages are numbered, headers are present, and while eBooks have a unique search function to locate particular phrases, the reader can't easily see it in the context of the entire text.

These features allude to the desired tactile experiences associated with reading that eReaders don't provide. A paper book offers a unique experience of touching, folding, and turning the paper. Material pages preserve an atmospheric smell throughout the years and make a distinctive sound when turned. So far, digital texts have not satisfyingly replicated this kind of tactility.

When picked up, a paper book reveals its weight, shape, and size, giving a reader an idea of the text's length. In contrast, an eReader weighs and looks the same no matter whether you are reading War and Peace or Winnie-the-Pooh. Researchers have found that these discrepancies based on touch create enough 'haptic dissonance' to discourage some people from using eReaders.

Underlining, highlighting, drawing, and leaving notes in the margins are tactile ways of interacting with a book that people have always enjoyed. Working on a project called The Archaeology of Reading in Early Modern Europe, academics looked at more than 400 books from the 16th and 17th centuries. They transcribed and translated what Renaissance scholars scribbled on the books they studied, concluding that marginalia reveal an accurate history of personal reading.

Electronic reading devices allow readers to highlight the text and share quotes easily online; electronic academic books also save the teachers' time on checking the exercises and prepare students for the digital world. Yet, paper books are still undoubtedly better for reading at bedtime and it will take a long time until eReaders recreate a similar sense of tactility, interaction, and smell of a paper book.

Art by Rahel Kiss

The psychological strains of COVID-19

How ongoing restrictions are taking a toll on the mental health of young people.

Written by Pauline Münchenberg

Shops, coffee houses and bars are closed; it is forbidden to meet friends and family; people are working and studying from home; many are feeling overwhelmed, anxious, lonely and stressed as society is struggling in its fight against a new virus. What sounds like a dark science fiction movie has become our sad reality.

The ongoing COVID-19 pandemic has taken a heavy toll on many of us. While restrictions focus on controlling the spread of the virus by protecting the most vulnerable, the number of people suffering from mental health problems has increased. Many are facing financial hardships or an existential crisis, questioning their place in life. Furthermore, a rise in domestic violence and child abuse has been observed: EU states have reported a 60% increase in emergency calls about domestic violence. Children and young adults in particular are struggling with ongoing social isolation, loneliness, and emotional distress, exacerbated by relentless monotony and boredom. In addition, the distribution of fake news across social media creates more fear. This has been painfully clear in the latest concerns over the AstraZeneca vaccine in many European countries, where misinformation, politics and vaccine skepticism have spread panic and hysteria across the continent. Furthermore, fears about the future and poor job prospects make this a time of anxiety for many young people.

In addition to health experts, the World Health Organization (WHO) has warned about the pandemic's mental health and psychosocial consequences. Due to self-isolation, an increase in depression, anxiety, substance abuse, sleeping problems and self-harm behaviour has been observed, as humans are social beings and have a basic need for social contact. Children all over the world are now experiencing loneliness and fear, compounded by high levels of parental stress and limited coping strategies. Those with pre-existing mental or physical health conditions or facing child or domestic abuse are particularly vulnerable to experiencing psychiatric symptoms. For example, studies in the UK, Ireland and the US have shown an increase in depression and trauma symptoms and generalised anxiety disorders during the pandemic, compared to before. Amongst other predictors, young age and female gender were associated with higher anxiety and depression rates. A meta-analysis conducted during an early stage of the pandemic in 2020 even suggested a pooled prevalence of depression that was seven times higher compared to 2017 in the overall population. These findings highlight the impact that COVID-19 has had on mental health.

The origin of most mental health disorders can be found in childhood or adolescence, as it marks an especially sensitive developmental period. A systematic review by the Great Ormond Street Hospital NHS Foundation Trust and UCL Great Ormond Street Institute of Child Health has shown that social isolation and loneliness increase the risk of depression in children and adolescents, while the duration of loneliness, rather than the intensity, is strongly correlated with symptoms of poor mental health. Therefore, the COVID-19 pandemic may not only

worsen existing mental health issues, but might also lead to more cases of ill health in children and adolescents.

As it turns out, one of the biggest barriers to solving this issue is the lack of mental health services. Schools and universities that usually provide these services are or have been closed, so getting access to care is much more difficult. Additionally, the abrupt disruption of services likely worsen mental health conditions. This is particularly true for disadvantaged groups who rely primarily on the care available in educational settings.

It is a time of uncertainty for everyone and each age group is facing its own unique challenges. While the issues of adults and the elderly are certainly important, it is crucial to remember that minors are also facing many challenges, particularly related to mental health. Current guidelines from the WHO advise us to take extra care of those in need, ourselves, and our loved ones. There is an urgent need to provide more mental health services: emotional and social support are key. Promising first steps in this direction include the rollout of digital healthcare services, so-called tele-health, such as online therapy, video consultations and mobile health apps. Furthermore, promoting exercise and mindfulness helps to improve psychological wellbeing and stress. Overall, the Government needs to focus more on the psychological strain of the pandemic and provide better access to treatment for those who require it. Corporations and employers can also play their part by offering mental health support strategies like yoga during lunchtime and by being flexible regarding the needs of their employees.

It is important to remember that it is okay not to be okay. And, crucially, everyone should be able to get help when needed.

Art by Sophie Maho Chan

The emergence of neuroanthropology: exploring the cultured brain

Are our brains a product of culture, or is our culture a product of our brains?

Written by Chrysi Anastasaki

The goal of neuroanthropology is to investigate the biological mechanisms and evolutionary processes that underpin our culture. Until recently, the connection between brain development and culture remained largely unexplored, but the integration of neuroscience and anthropology is starting to provide fresh insights on the matter. This has the potential to answer exciting questions, including: are our brains a product of culture or is our culture a product of our brains?

Anthropologists try to understand why humans behave the way that we do. They study human behaviour and social life, using symbols, historical evidence, and practices of different cultures. On the other hand, neuroscientists are interested in how our brains work. They study the structures in the brain, using a variety of experimental and observational methods, with the aim of understanding cognitive function. Neuroscientists use tools including behavioural tests and imaging techniques, such as MRI.

There is substantial evidence to suggest that culture is linked to neural activity: from low-level perception and attention to high-level language production, calculation, music, emotion or self-awareness. Thus, neuroanthropology provides a novel lens by which researchers can distinguish and compare neurological mechanisms that are associated (or not) with cultural behaviours. To explore this in more detail, let's take a look at three human evolutionary practices: emotions, rituals and human kinship.

Emotion is central to culture and its expression relies extensively on language production. In Japanese, the term 'amae' refers to the desire to be socially dependent on others. In Micronesia, the Ifaluk civilization uses the word 'fago', which refers to a loving, empathetic form of compassion. An example of 'fago' is when a caring mother tends to her sick child. Often, words such as 'amae' and 'fago' do not have a direct English analogue, so it would be useful to create behavioural experiments for native speakers of these languages containing such words as stimuli. This would enable researchers to identify the areas of activation for these words and determine whether they have distinctive neural pathways.

Furthermore, some anthropologists claim that rituals are the foundation of human socialisation. They require contribution from diverse aspects of cognition, ranging from the processing of multi-sensory stimuli to motor skills, symbolic learning and emotional memory. Some of these aspects have been linked to certain brain structures thanks to the results of neuroimaging studies. For example, the amygdala is a tiny, almond-shaped area of the brain, and scientists have demonstrated that it responds to emotions, including fear, disgust, and anger. Further studies linking neuroimaging experiments with anthropological practices such as rituals could allow scientists to study activation in regions, including the amygdala, to enhance our understanding of how emotional memories are processed in different cultures.

Furthermore, Dr Joan Miller, Professor of Psychology at the New School for Social Research, compared the ethnography of kinship (how family relationships are structured across different nations) between groups of people from Tamil Indian and British populations. This study showed that in the British kinship system, the father's brother and the mother's brother are considered 'uncle' and are equal to each other but less powerful than the father of the family. In Tamil Indian families, however, the father's brother has the same power as the father (they are both called 'appa') while the mother's brother is called 'maman'. Some scientists speculate that these differences in kinship reflect cultural differences in brain structure or

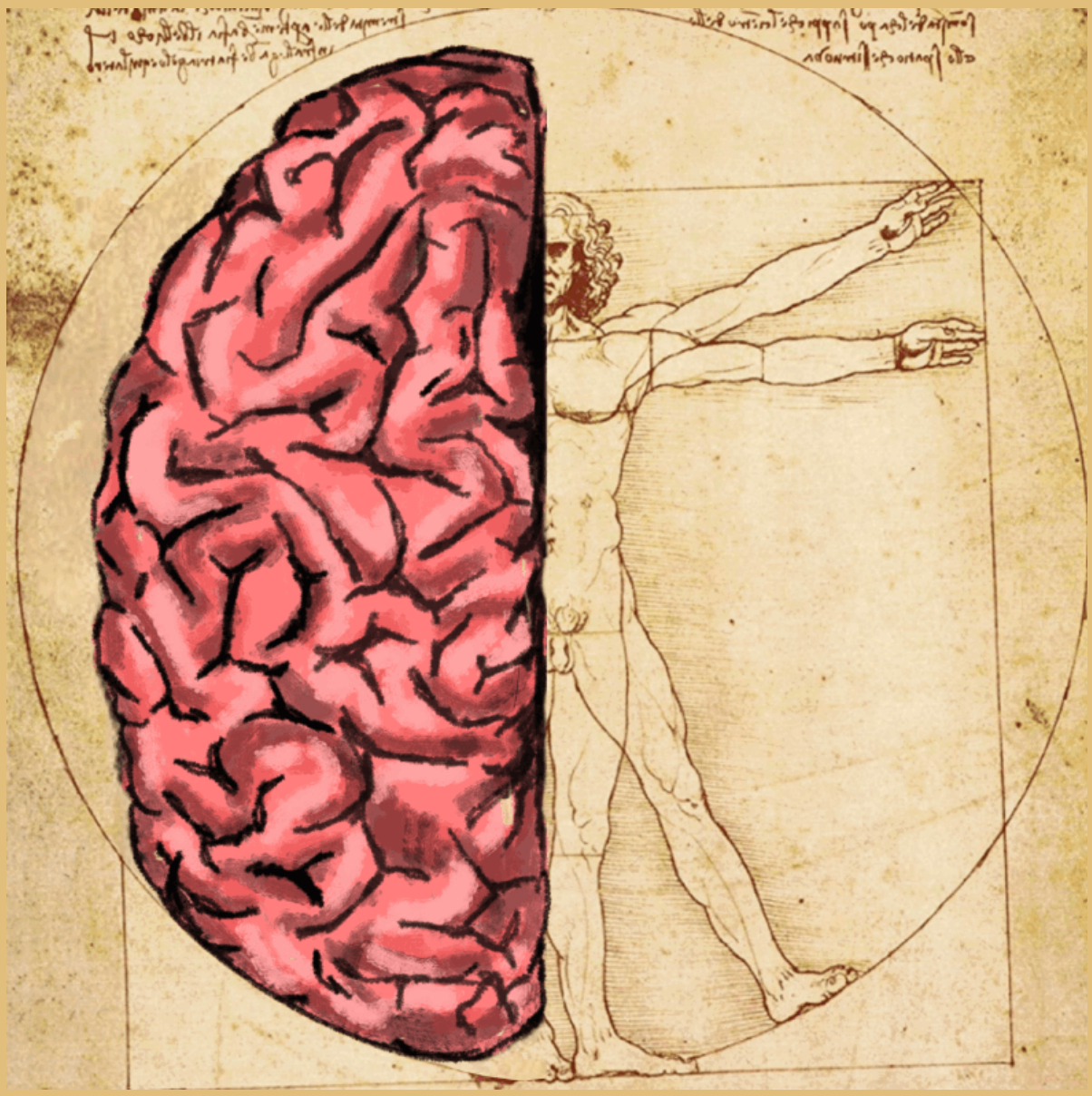
even neural activation. Neuroimaging techniques can be deployed during behavioural experiments, such as face recognition for different relatives, to identify trends and allow neuroanthropologists to investigate these ideas further.

It would also be interesting if this new field of neuroanthropology could be used to examine the long-lasting debate of nurture versus nature. In one of the most popular modern books on the subject, The Encultured Brain, editors Lende and Downey explain that deep enculturation refers to the long-term adaptation of neural systems to cultural concepts until they become 'neurological anatomy'. It seems that both nature (our brain and our nervous system) and nurture (the culture we are brought up in) shape human evolution and development.

Even though neuroanthropology is a fascinating new research field, it is important to consider its limitations. The lack of suitable experimental methods forces the field to rely extensively on interdisciplinarity and brave testing attempts. Also, researchers are invited to bridge the gap between their own knowledge and culture and the culture that it is examined, which is often a challenging task.

Overall, the combination of anthropology and neuroscience is creating a new toolkit that will help scientists to conduct experiments in order to investigate the cultural element of our brains, such as emotion, ritualistic behaviour and the structure of kinship in families. This enriches our theoretical and biological understanding of the human brain. It will also contribute to our understanding of societal issues, such as intercultural awareness and education, and could even be used to inform policy.

Art by Lola Artiles



Nanobodies - small, but oh my

Re-evolutionizing the antique immunology toolbox of llamas, sharks & co.

Written by Annika Schulz
Art by Stephanie Chang

Towards the end of the 20th century, an astonishing finding was made in camelid and shark blood serum. Sharks are known to have evolved the earliest form of adaptive immunity, whereby immunological memory can be generated and pathogens targeted with high specificity. In these animals, a previously unknown miniature form of antibody was discovered to form part of their adaptive immune system. Similarly, these small antibodies have also been identified in quite different vertebrates like camelids, which includes camels, llamas and alpacas.

Structurally, conventional antibodies are Y-shaped multimeric proteins consisting of a homodimeric heavy-chain and two light-chains that attach at the small arms of the Y-shape. However, in serum from nurse sharks or llamas, you will also find antibodies possessing just the heavy-chains made up of a single variable domain and two (camelids) to five (sharks) constant domains. While not much is known about how these seemingly incomplete structures emerged in distantly related species, their discovery has certainly provided a stepping stone for a wide range of biomedical research endeavours.

So what does a heavy-chain-only antibody possibly have to offer? The extensive repertoire of antigen-binding sites generated by these smaller antibodies in camels suggests they are not the result of faulty design. Instead, by isolating the single variable domain from heavy-chain-only antibodies, minute structures known as nanobodies were created. Being the smallest known antibody fragment capable of antigen binding, these nanobodies have their own methods of creating binding specificity and diversity.

A variable domain commonly consists of three complementary determining regions (CDRs). Of these, the CDR3 loop region is thought to play the most important role in antigen binding. That said, nanobodies possess an extended CDR3 loop, which allows them to reach unique target epitopes inaccessible to their shorter counterparts in antibodies. Nanobodies also don't limit their antigen-binding capacity to the loop regions, thereby even offering a greater diversity of antigen-binding sites than classical antibodies. These phenomenal characteristics, in addition to high-yield production in E. coli biofactories, open up a range of applications in cutting-edge research across the board.

In the lab…

One of the most significant achievements to date that involved the use of nanobodies was the determination of the human β2 adrenergic receptor (ADRB2) structure. In 2012, Brian Kobilka received the Nobel Prize in Chemistry for his contribution. Using nanobodies, his lab was able to lock ADRB2 in its active state to obtain a crystal structure. Other fragments from regular antibodies had previously failed to stabilise the receptor but with the significantly smaller nanobodies, they obtained

sufficient data to solve it. Today ADRB2 is a well-defined member of the 7-transmembrane receptor class, which forms the target of a major proportion of currently approved drugs.

In diagnostics…

A significant challenge in the field of cancer imaging is the poor penetration exhibited by classical antibodies used to deliver visualisation agents. Nanobodies overcome this problem by offering higher levels of tissue penetration while staying in the body for a minimal period of time, since they are rapidly filtered out by the kidneys due to their small size (notably, this can be modified for therapeutic purposes). This also makes them a good probe for tumour type detection. For instance, a phase II clinical trial will be completed this year investigating the efficacy of nanobody-based detection of HER2 expression in breast cancer. What is more, nanobodies have excellent properties for rapid diagnostic assays used to identify infectious agents. They are very heat-stable compared to antibodies, which has major implications for diagnostic testing in settings lacking appropriate refrigeration facilities.

In patients…

Over past decades, the use of monoclonal antibodies as drugs has seen a dramatic increase. Nanobodies offer these therapies novel prospects with enhanced efficacy and administrative advantages. For instance, nanobodies with two different antigen-binding sites fused together have been shown to inhibit solid tumour growth. However, given the lack of the heavy-chain constant domain, nanobodies don't elicit the same immunological effects as classical antibodies.

That said, nanobodies can be employed advantageously to modulate inflammation in other ways. For example, rheumatoid arthritis and inflammatory bowel disease management includes anti-cytokine antibody therapies. These are delivered by intravenous infusions but with the more robust, heat- and acid-stable nanobodies, these treatments could potentially be delivered by inhalation or orally. A novel antiviral therapy for rotavirus based on the orally administered nanobody ARP1 was found to be effective in controlling viral diarrhoea in infants. Further developments envision delivering ARP1 in the form of immunity-boosting functional foods like rice.

What's next?

In the lab, nanobodies will soon lend a helping hand to CRISPR technologies to enable the control of gene expression and epigenetic memory without causing DNA breakage. Recently, multivalent nanobodies have also been put forward for the development of desperately needed therapies for COVID-19. SARS-CoV-2 neutralising nanobodies work by not only interfering with viral receptor binding, but may also induce conformational changes that prematurely activate fusion machinery. Multivalent nanobodies provide fantastic prospects for reducing mutational escape of the virus and could even be administered by inhalation.

How odd to think this all started with the discovery of seemingly flawed antibody isotypes in camelids and sharks…

Beyond the vaccines: messenger RNA's role in tomorrow's therapeutics

Whilst the COVID-19 pandemic has provided an unparalleled set of challenges for society, the advent of RNA vaccinations has given us a glimpse of the potential for a brand new class of therapeutics.

Written by Julian Grinsted

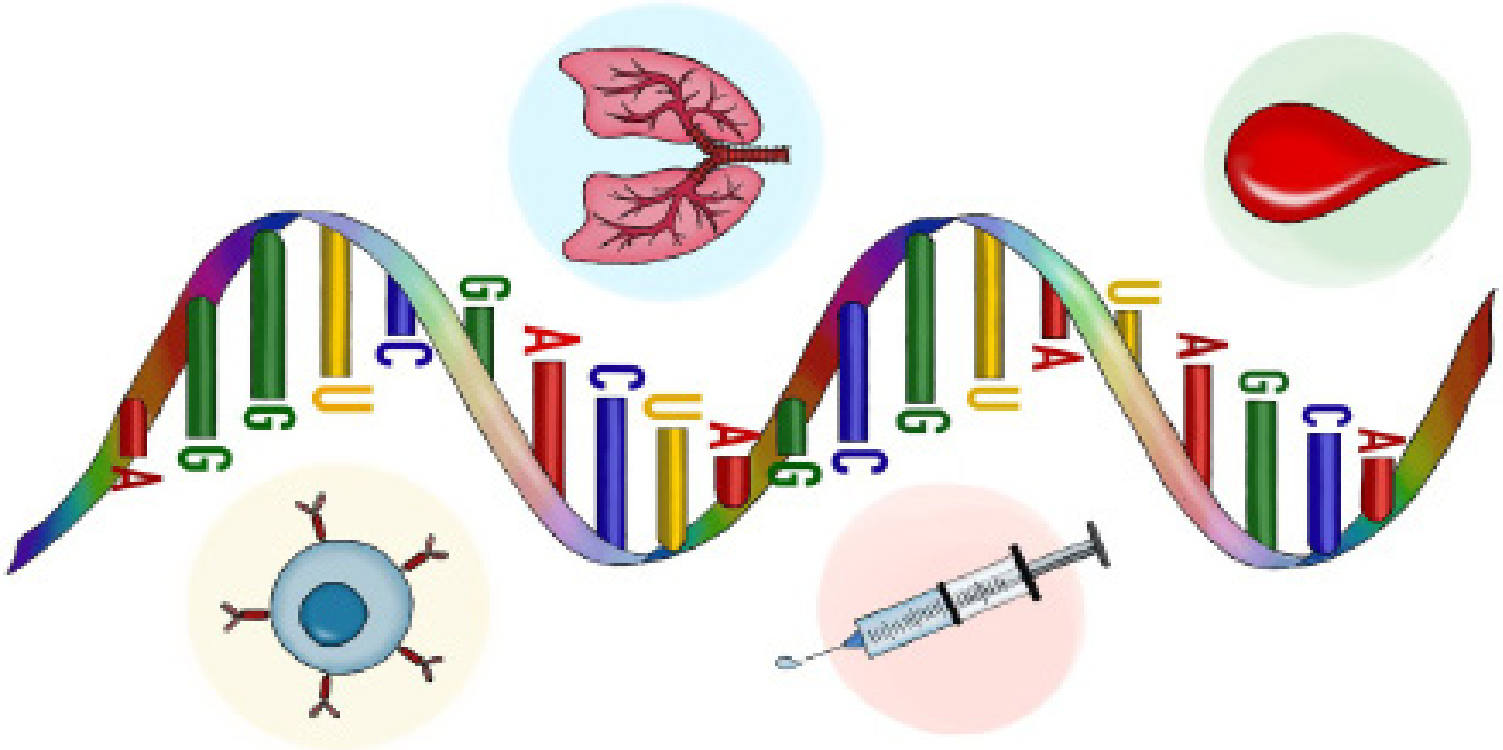
CRISPR-Cas9, Standing for Clustered Regularly Interspaced Short Palindromic Repeats, is a new and exciting gene editing method. It enables a change to an organism's genome in a method that is cheaper, faster, more accurate and very efficient. A human-created piece of CRISPR RNAs (transcribed from CRISPR sequences) binds to a targeted area of DNA and the Cas9 enzyme. while The modified RNA recognizes the DNA sequence, and the Cas9 enzyme cuts the targeted location of DNA. Afterwards, the cell's own DNA repair system is used to add, delete or change pieces of genetic material. In other words, CRISPR RNA identifies old DNA and places it with the new genetic material while the Cas9 enzyme cuts the old DNA out.

CRISPR can be used in healthcare, to fight bacteria and viruses such as HIV, where vaccines fail. Immunologist Dr. Justin Taylor and his colleagues in their preprint for a journal said that using CRISPR to edit B cells could produce "immunity against pathogens for which traditional vaccination has failed." Changing the coding of the B-cells (protective cells) in their DNA could make them stronger and better adapted to create antibodies to fight viruses and bacterias. It would be is an efficient and permanent way of immunizing human body against viruses and bacterias. "We can see gene editing [to protect against viruses] becoming feasible," said Dan Wattendorf, director of Innovative Technology Solutions at the Gates Foundation. These new ways of using CRISPR opens up a whole new world of healthcare and medical development.

CRISPR has other implementations in everyday life beyond fighting against viruses: it can be utilized to change characteristics of the human body. Josiah Zayner, a former NASA biochemist, became the first person to use CRISPR to change their own genes. He owns a company called ODIN that sells DIY (do it yourself) CRISPR kits, basically starter kits for gene editing, to include a free guide for anyone wanting to experiment on themselves. He live-streamed an event, injecting himself on the arm with CRISPR that (theoretically) enhanced his muscles by editing the gene for myostatin, a protein that regulates muscle growth. There is still no exact data showing the changes of his cells; however he said that he is working on developing assays to try to detect that. Anyone can buy the kit that he used to inject himself with CRISPR for myostatin or other kits that enhances the human body.

However, many problems arise if anyone can buy these DIY kits; some people take it to the extreme by using CRISPR in a not scientific and dangerous way. Zayner believes that people should base their actions on scientific data by saying "Be knowledgeable!" Even though Zayner thinks that people should be careful, he puts his confidence in expanding the usage & research on CRISPR with these sets. He says to the Atlantic: "It [academic and medical science] won't be available to the general public for 10, 20, 30, 40 years...How do you expect this technology go forward if they aren't testing, playing around it?" With his words, he shows his frustration that in order for a technology to be developed it should be more accessible.

Art byKate Mourling



An interview with Professor Nick Lane, an evolutionary biochemist and award-winning writer

On how energy flow has shaped life on Earth and how writing books has shaped his research

Written by Sophie Maho Chan

Professor Nick Lane is an evolutionary biochemist at the Department of Genetics, Evolution and Environment at UCL. In addition to being the co-founder of UCL Consortium for Mitochondrial Research and co-director of the UCL Centre for Life's Origin and Evolution, he is an author of four acclaimed books. This includes Life Ascending, which won the 2010 Royal Society Prize for Science Books.

"I think it's really helpful for writers to keep a foot in science and I think it's really helpful for scientists to keep a foot in writing. The two go hand-in-hand."

Energy flow and evolution is the common theme running through Prof Lane's research. He points out that the history of life on Earth is "very weird" and cannot be fully explained by genes alone. Specifically, prokaryotes – single-celled bacteria and archaea – arose 4 billion years ago and have stayed in their 'simple' form ever since. In contrast, 'complex' eukaryotic organisms – including everything from humans to amoeba – can all be traced back to a common ancestor that arose just once around 1.5 to 2 billion years ago. While the commonalities between animals, plants, fungi and amoebas may not be apparent at first glance, we share a surprising number of features that distinguish us from prokaryotes, including the presence of a nucleus, sex and ageing. As Prof Lane puts it, there is a "gulf of difference" between eukaryotes and prokaryotes. The question is why and how can we explain these fundamental universally shared traits.

To this, he answers energy.

"Anybody who goes into researching evolution is bringing their training… I'm bringing my day job in because my PhD relates to bioenergetics". While recognising that this comes with the danger of subjectivity, the fact that all life is driven by the peculiar mechanism of electrical charges across membranes reaffirms the centrality of energy to life. Drawing on mathematical modelling and biochemical experiments, Prof Lane argues that throughout evolutionary history, the energy requirement of life has placed constraints on trajectories of natural selection. By appreciating energy's "explanatory power", we can unpack major evolutionary transitions, from the very origins of life to why eukaryotes evolved sex and ageing.

When questioned about what sparked his unique bioenergetic perspective on evolution, Prof Lane has an unorthodox story to tell. "Well… writing books."

After earning his PhD investigating what goes wrong with mitochondria in kidney transplants, Prof Lane went on to reconcile his long-held passion for writing by taking up medical writing jobs. He eventually found himself in a 'creative' medical communications agency, writing storylines to accompany video animations about how drugs work.

"I learned a lot about writing from doing that," he recalls. One lesson was the need to write about science as a straight narrative, which, he reflects, made him "deal with causality in a really direct way". Another key takeaway was the importance of writing in plain English, especially in catering to a diverse audience of healthcare professionals and patients. He recounts how he had long internalised that good writing equated to complicated words and sophisticated prose. While admitting a chronic urge to still write in flowery passages, he says that he now values plain English. "Let the science do the talking, not the words."

Prof Lane's life came into a full circle when he embarked on a journey to write his first book, which started off being about free radical chemistry, a subject matter he took a keen interest in during his PhD. As he explains, however, the book "took a life on its own". Oxygen: The Molecule that Made the World, explores not only the medical implications of oxygen but also its geological origins and how it influenced evolution, from the origins of animals to why we age. He describes the fun in learning about something completely outside of his comfort zone and how it broadened his view to look at big evolutionary questions from a biochemical standpoint. Long story short, he found himself back in academia, addressing the same big questions in his books in the lab himself.

"I did it the wrong way round… well, I would even say the right way round – except that there isn't a career structure that allows people to leave academia and come back in."

According to Prof Lane, his writing

Art by Olivia Kehoe

informs his research. Given the scope to explore disparate fields and competing theories in books, he gained the confidence to have opinions on big questions, even if they are wrong. Accompanying this, he developed a sense of moral duty in conveying his work honestly. "People read and trust what you say," he explains. "I can't just say anything I want… [there's] a requirement to be honest about other people's work even if it contradicts yours and guiding people where you are going and why… which is actually a really valuable training as a scientist."

When asked about what it means to communicate his work, he says, "It's a thrill". From where he sees it, most people are inherently interested in big questions about life and therefore willing to go to great lengths to understand complex science, given sufficient confidence that what they are reading is worth reading. This is why he tries to incorporate contexts, histories and humour to inject some "humanity" into his writing. While he recognises that most people may think his books are demanding, he emphasises trying to capture the threshold of minimal explanation for the maximum effect.

GLOBAL MEDICAL CITIZENSHIP IN LIGHT OF RISING NATIONALISM

Governments around the world have valued their own interests with utmost priority in their COVID-19 response, but at what cost?

Written by Lia Bote

The COVID-19 pandemic has tested the resilience of our social and political systems, inviting many significant changes. One such change is the resurgence of nationalism, the belief that one's nation should occupy greater socio-political importance than others. This is coupled with deglobalisation, which although key to reducing international transmission of SARS-CoV-2, has posed new challenges. Specifically, medical nationalism has seen public health policies and allocation of medical resources prioritise a country's own needs, regardless of wider global repercussions. This was seen in the EU at the beginning of the pandemic, where restrictions on the export of medical supplies resulted in shortages of equipment elsewhere. Thus, the resurgence of nationalism and the resulting limitations to freedom and information have resulted in a less collaborative, less cooperative global medical field.

Often, the unfortunate price of self-preservation is the neglect of anything that is 'other'. Migrant workers comprise 14% of Europe's working population. For key workers, the number is even higher, with immigrants making up 23% of doctors in major cities. Despite this, migrant workers are also some of the least protected. In the name of nationalism, governments have prioritised the safety and security of their own citizens. As a result, migrant workers have been the first to lose their jobs, and are often forced into unsafe and unsanitary working conditions. This is true across the globe, with COVID-19 outbreaks in Malaysia or Singapore starting at crowded dormitories where migrant labourers are forced to stay.

But is a strong national identity always harmful? The COVID-SCORE was an international survey that measured people's satisfaction with their government's pandemic response, evaluated on criteria like medical preparedness and international cooperation. There was a positive correlation between satisfaction and government trust, which resulted in higher degrees of compliance. As such, countries with higher average scores also had better responses to COVID-19 when measured through metrics like mortality rates and survey respondents having relatives who had been infected. This makes the case for the value of a strong sense of national unity. In fact, the highest satisfaction measures with lowest heterogeneity among respondents were in countries like China and South Korea with strong nationalist policies. In contrast, the US had the highest heterogeneity and a weaker central response, where the lowest-earning demographics reported lower satisfaction measures.

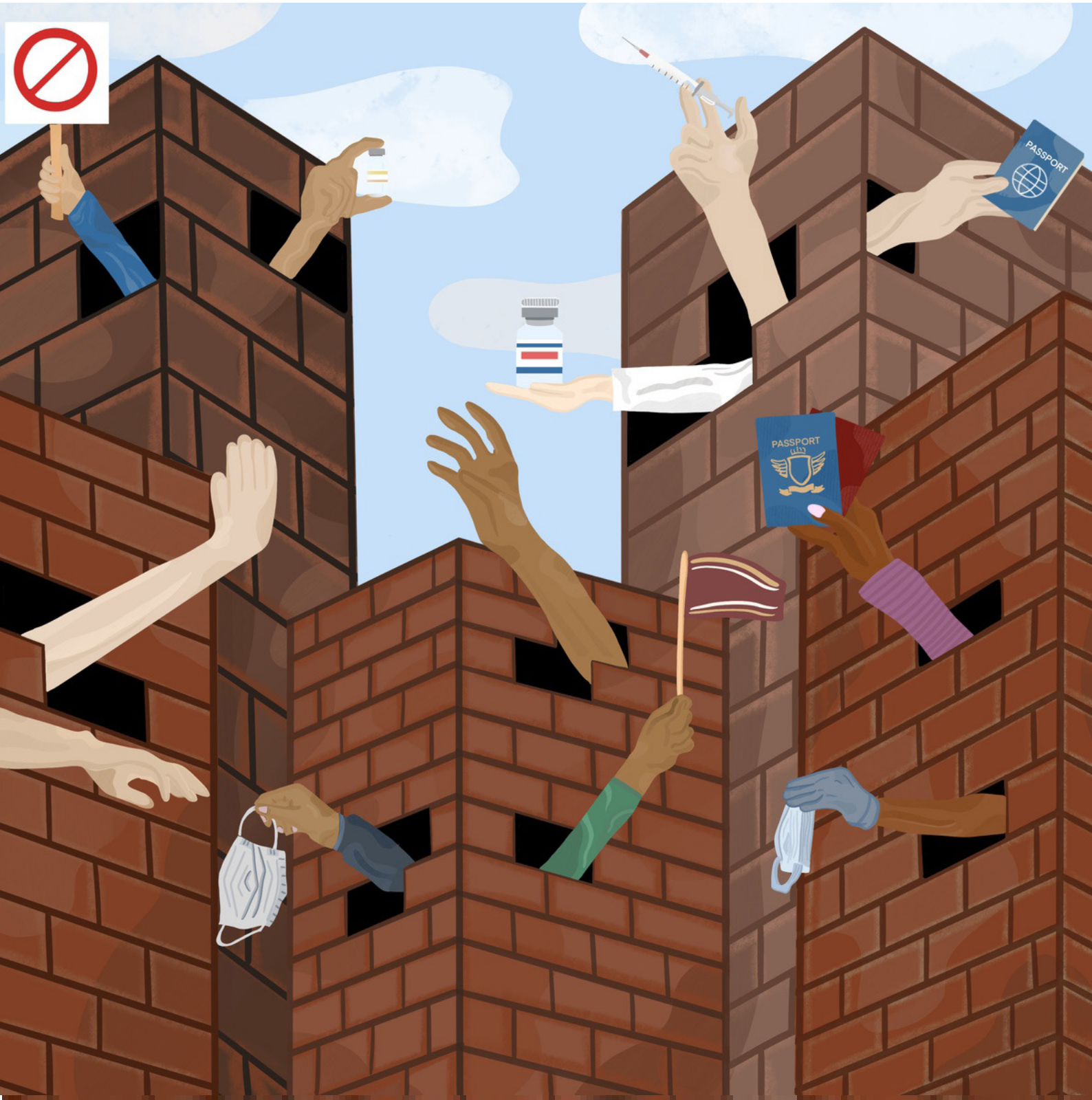
Still, strong government responses need not be mutually exclusive with international cooperation. Economic and socio-political forces will not allow borders to remain closed forever, but unless COVID-19 is eradicated everywhere, it cannot really be eradicated anywhere. This is perhaps best exemplified by the problems arising from vaccine distribution. Countries like Germany plan to vaccinate their population entirely by the summer, while Sudan and others will likely not achieve this until 2024. The UK has vaccinated 50 people in every hundred as of March 2021, which is well above the world average of 7%. Moreover, over 130 countries have not received their first vaccines yet, while just 10 countries have administered 75% of the world's current available doses.

International programmes to address this and promote global medical cooperation have been met with limited success. The World Health Organization's (WHO) COVID-19 Technology Access Pool repository was launched to allow companies to share their manufacturing and research knowledge. The major vaccine producers have expressed support for this but are yet to join. Canada, which has vaccinated

62% of its healthcare workers, and has enough vaccine orders to inoculate its adult population five times over, has taken vaccines from the Covax scheme, which aims to pool resources from higher income countries for vaccine distribution to low- and middle-income countries. The result is widening global health inequalities in the name of self-preservation.

It does us a disservice to think of health crises as isolated from the social contexts within which they exist. Effectively managing the pandemic relies on a degree of international cooperation that, at present, seems to be as far from reach as the end of the pandemic itself. In an increasingly interconnected world, global health solutions must be human solutions, because the only way out of the pandemic is if we can get out of it together.

Art by Sophie Maho Chan



COVID-19: Lessons learnt?

Will we be better prepared for a future pandemic after COVID-19?

Written by Niru Varma

In the wake of the 2015 Ebola crisis, then Prime Minister David Cameron used the G7 summit as an opportunity to call on Britain and the world to "wake up to the threat" of disease outbreaks, and laid out a plan to ensure the UK was as prepared for a future pandemic as possible. This included investments in drug research and development, greater transparency in research, and improved protocols and dedicated staff for rapid response to outbreaks. Looking back almost six years later, amid the very crisis anticipated, it is easy to question how effective these measures really were. Cameron himself admitted earlier this year that much of their planning relied on the assumption of an influenza outbreak, with insufficient attention being paid to other possibilities, saying that "More should have been learnt from the experience with SARS and respiratory disease in terms of our own preparedness." Indeed, the success of many Asian countries in controlling the spread of COVID-19 has been attributed to protocols already established following previous respiratory disease epidemics.

The flaw in the pandemic preparation strategy of countries like the UK and the US is that respiratory diseases, like SARS and COVID-19, require vastly different mitigation measures to influenza. Quarantining and contact tracing those with symptoms and the people they come into contact with is an effective way of controlling respiratory diseases. It is less effective for influenza, which has a highly infectious period that precedes the symptomatic period - the only possible response is mitigation, not full suppression. It is believed that the UK Government's initial COVID-19 pandemic response was informed by their influenza preparedness strategy; they were not prepared for the measures required to suppress the virus rather than simply mitigate transmission. Meanwhile, countries like Singapore and South Korea had far lower rates of infection and disruption as a result of the pandemic, having prepared for the correct scenario.

With the frequency of pandemics likely to increase as human behaviour makes us more susceptible to them, Cameron's call to increase our preparedness only becomes more relevant. As World Health Organization (WHO) Director General Dr Tedros Adhanom Ghebreyesus states, "For too long the world has operated on a cycle of panic and neglect. We throw money at one epidemic and when it's over, we forget about it and do nothing to prevent the next one."

When looking into future pandemic mitigation, it is important to understand the causes. Human behaviour is one large driver; as the world becomes more global, with ever increasing rates of transport of people and cargo, the risk of an outbreak turning into a worldwide pandemic always rises. The outbreaks themselves can also be attributed to human intervention. The vast majority of new disease outbreaks occur as a result of zoonoses – animal diseases that make the jump to infect humans. The COVID-19 pandemic was transmitted from a bat, the natural host. Nipah virus from bats, swine flu from pigs, and MERS from camels are three other zoonotic diseases on scientists' watchlists of future epidemic and pandemic concerns. Inevitably, the chance of zoonotic transmission of a disease increases greatly with the amount of contact humans have with animal carriers – invasion and destruction of habitats and livestock farming all contribute to this. Movement of livestock around the world also facilitates spread. Monitoring of animal populations, identifying routes of transmission, and screening animals for new diseases and variants play a vital part in preventing outbreaks that may lead to pandemics. Eventually, another pandemic outbreak is almost inevitable – however, identifying these outbreaks early can still help with early management and mitigation.

If the next pandemic turns out to be another respiratory virus, we would hope our government at the time would be somewhat better prepared simply from experience. Turning back to SARS, it is easy to praise the performance of the governments who apparently learnt their lessons from this disease. However, the fact that they were prepared for the right pandemic does not mean that they would necessarily be better prepared for a different pandemic. The seemingly obvious lesson to be observed here: any future strategy must account for more than one possible disease scenario, and must not assume that strategies are interchangeable.

But of course, 'prepare better' is easier said than done. The details of how exactly to prepare better, especially for different pandemic scenarios, is less clear. Breaking the so-called 'panic-then-forget' cycle is a topic of acute interest to the WHO and many world leaders. In October 2020, the UK Health and Social Care and Science and Technology Select Committees launched a joint inquiry into the lessons learnt from the COVID-19 response. The inquiry considered, amongst other things, the UK's

Art by Grace Gu

prior preparedness for this pandemic, and the effectiveness and deployment of interventions and management strategies. Publication of a final report is still pending, but whatever the outcome is, preparedness for a future global health emergency will involve more than just planning for specific pandemic scenarios. Many argue that COVID-19 simply shone a light, in the most disruptive way, on existing flaws in our infrastructure, healthcare, and general way of life. Papering these cracks will require long term preparation – something our political system is not catered to. Our governments are not used to thinking beyond the short term – or, more accurately, the five year term. The 'panic-then-forget' cycle seems like an inevitable constant, the question of lessons we can learn a bleak one. All we can do is take advantage of pandemic prevention being in the public eye to push for greater funding into public health, infectious disease research, and healthcare, as well as much needed healthcare and social care reform.

Living forever? It's written in your DNA.

The prospect of being immortal might be closer than we think.

Written by Maja Bronowska

The idea of living forever may sound insane. There is no doubt that we age, and that our biological functions decline leading, eventually, to death. Human life expectancy has extended enormously and continues to increase, but is there a limit? The answer is unclear. The oldest documented human, Jeanne Calment, lived for 122 years and 164 days, dying in 1997. For over two decades, this record has persisted. In general, human longevity records no longer increase, as if having reached a plateau.

Undeniably, our society is ageing. It is estimated that by 2037, 1.37 billion households will be headed by someone 85 years old or older, an increase of 161% from now. As a consequence, this will drive up health and social healthcare costs, increasing the burden on taxpayers and the care system. With age, biological functions decline and societal roles change. Moreover, avoiding environmental diseases and improving chronic health conditions cannot extend longevity forever. The real culprit that must be overcome is ageing itself.

The blueprint of ageing is held within DNA, and so the maximum achievable age is mostly determined by genetics. Using genomic techniques such as next-generation sequencing, gene variants of APOE and FOXO3A were found to be highly associated with longevity in humans. The APOE gene is associated with Alzheimer's disease whereas FOXO3A was found to play an important role in carcinogenesis. However, the suggestion that these two genes alone are the strongest drivers of longevity in humans remains controversial. Ageing is more likely the product of complex interactions between many genes.

Furthermore, genomic stability plays an important role in ageing. Stability depends on DNA integrity, which is maintained by DNA repair mechanisms. This supports the proposition that it is the interaction of many genes, rather than a handful, that is responsible for ageing. Nonetheless, gene expression is not solely genetic, but is a combination of both genes and environmental factors. Epigenetics, the study of how environmental factors alter gene expression, is quickly becoming an essential area of knowledge in science, allowing us to understand more about patterns of gene expression and how they are regulated.

Ageing is likely linked to epigenetic alterations, particularly DNA methylation. At cytosine-phosphate-guanine (CpG) DNA sites, methyl groups covalently bind to cytosine, leading to altered expression of genes, including those that are critical for ageing, without altering the original DNA sequence. These methylation patterns change with age and can be considered as 'clock' biomarkers that track ageing with high accuracy.

In 2019, Benjamin Mayne and colleagues carried out a study in which they analysed the density of CpG sites in the genomes of vertebrates with established lifespans. CpG islands are prone to mutations, suggesting that they may be involved in evolutionary processes. They found that 42 gene promoters can be used as effective biomarkers to assess and predict the lifespans of different species.

Surprisingly, for humans, the lifespan clock is estimated at 38 years. Analysing trends in life expectancy and late-life survival, we see that women tend to live longer, but there is a sharp decline after the age of 80. Ageing can be considered as a series of pre-programmed events to enforce natural selection, but, in the case of humans with advanced medicine at our disposal, this is no longer the case.

In particular, our understanding of epigenetics has improved enormously. Epigenetic aberrations responsible for genomic instability in cancer patients are now targetable. New generations of drugs that are highly selective are

entering clinical development phases. Once we master this, it might be a matter of time before the same approach is applied to ageing. Some pharmaceutical interventions have already been demonstrated to improve life expectancy, so the possibility of altering gene sequences is even more promising – particularly with adeno-associated viruses or CRISPR/Cas9 systems.

Together with advances in science and our understanding of longevity, ethical considerations are also being raised. Many scientists point out that immortality poses a threat to our society. The overpopulation crisis may lead to shortage of resources. 'Life extension' technologies are likely to be expensive, making them a luxury for the wealthy and exacerbating inequality.

The idea of clipping genes that reduce our longevity and introducing alleles that can extend our lifespan is tempting. As for today, it is not possible yet, but it is not too distant a reality. New technologies are emerging and gene editing technologies are developing faster than we may expect. Thus, the way we think about life and death is soon to be changed. Naturally, we want to keep on extending our lifespan, but the remaining question is: who wants to live forever?

Art by Zach Ng

The Many Challenges of Kew Gardens' Tree of Life Project

Reflecting on the aims of an ambitious plan and the thorny challenges therein.

Written by Joshua Williams

A 2016 Kew report estimated the known number of currently existing plant species to be just under four hundred thousand. Since then, one branch of their Plant and Fungal Tree of Life project (PAFTOL) has sought to understand the evolutionary relationships in this incredibly diverse group. The project envisions a powerful collaborative resource, one that is flexible, reproducible, and contains high quality, up-to-date information.

This inspiring goal was set out in a 2018 roadmap publication in the American Journal of Botany, which identified both the key requirements in a set of calls to action, as well as potential challenges. Such obstacles face not only this project, but reflect the broader difficulties of bringing large numbers of people and organisations together with a common goal. In this way, the many considerations here serve as food for thought for a wide range of endeavours, scientific or not.

Firstly, the project must cater to a number of varied use-cases depending on the experience and role of the user. The data should be accessible to both unspecialised users such as educators who might require just a basic phylogenetic tree, as well as for specialist researchers, integrating external tools for detailed tree modification and customisation.

The project also needs to be accessible – if the data are unavailable to certain users (for example, by having a steep paywall) then the project will struggle to take hold globally. Furthermore, opening the data to all will encourage greater education and thus promote interest, creating a positive feedback loop to support a new wave of research, especially crucial for current global challenges like food security. This accessibility extends to use of the resource. Navigation should be intuitive, and technical details clearly annotated for non-specialists. Adequate guidance and help for newcomers to the resource should be easy to find and building a large community would encourage the sharing of techniques and ideas to further improve the resource.

Principle amongst the challenges is the continual upkeep of such a database since it would be a tragic loss for such concerted effort to go to waste as soon as the project's funding ended. Project leaders suggest the need for constant funding from institutions worldwide to ensure the effective upkeep of the resource following its creation, something undoubtedly difficult to secure. The project is proposed for the greater good of research, rising above competitive and monetary interests, but without these there may be lack of motivation for funding bodies to support the efforts.

Additionally, the project needs either to resolve or make clear conflicts in the literature, as well as demonstrating lack of knowledge in some cases. Along with this, it will be necessary to dedicate resources to moderating and validation of phylogenetic trees, computationally and/ or manually, since errors or missing data could have major consequences for further research.

This leads to the issue of data continuity. Not only do different geographic regions, institutions and even labs store data in different formats, but additionally different genomic markers are often used in phylogenetic studies. Since reconstruction of phylogenetic trees relies on comparison of genetic markers between the species, a lack of prior consensus on these markers means many of the previously studied species will have to be re-analysed. Whilst this is not entirely redundant, it will surely slow the project's progress.

A final challenge for the project is the need to design new algorithms for phylogeny. Much of the software currently used cannot accurately handle the hundreds of thousands of species necessary for this project. More importantly, if these algorithms disagree with existing studies about the placement of individual species or taxa, there must be processes to absolve these disagreements whilst retaining the integrity of the algorithm as a whole.

In February 2021, the first data release of the project was published, reporting a phylogenomic dataset of 3099 angiosperm samples, the most extensive of any such database to date, with members from 96% of known families and from all 64 orders. This work is presented in an open data portal named the Kew Tree of Life Explorer and serves as an impressive precedent for future work to follow.

As an overview, the project lays out a pipeline of steps which involve gathering data online, studying it for phylogenetic reconstruction, storing it securely and efficiently, and then presenting it for public use. Each stage of the process presents a huge and challenging task, but I hope that the project finds success, as this sort of centralisation will be invaluable for efficient progress in a broad range of plant sciences research, as well as paving the way for similar projects in other phyla.

Art by Sophie North

The Colour Palette of Biology and Model Deception

Scientists frequently employ personalised models to communicate their work; could this lead to misconceptions in biology?

Written by Marie Emilie Maeland

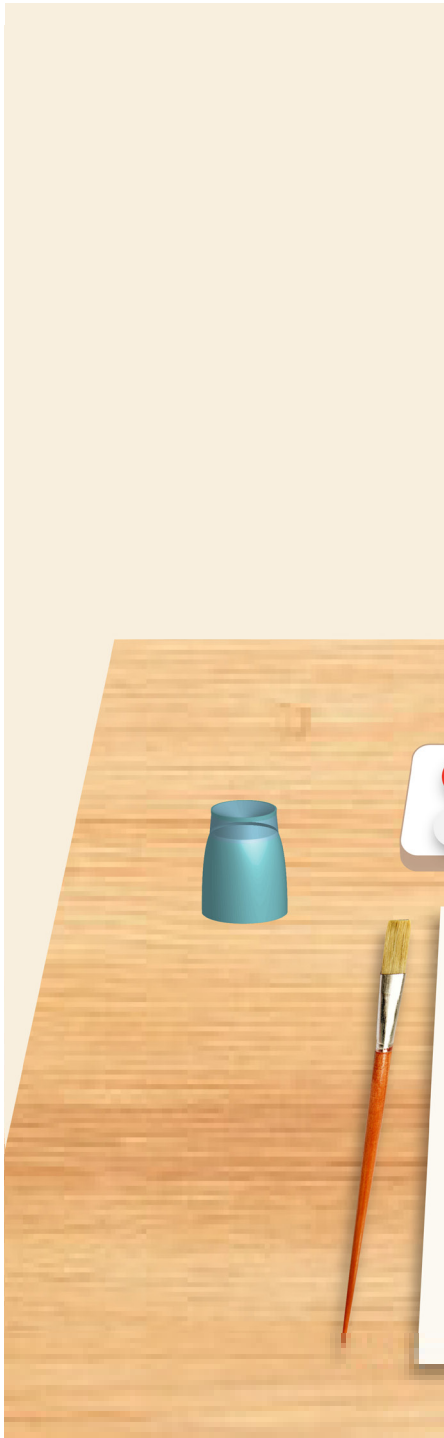
An artist's palette for biology extends from molecular laboratories into global media sources, such as Nature News and Science Magazine, who publish articles based on the latest research. Scientists aim to make their research understandable through models, often decorated, personalised and coloured for a global audience with scientific interest. Have their attempts succeeded or created unnoticed misconceptions in biology?

Colour has been linked to learning and memory. Once an association with a colour is made, it is likely to ameliorate the chances of recall. This has encouraged us to assign colours to the molecular universe that might originally only be visible to the human eye in black and white. Colouring systems have relatively recently become useful ways to understand microscopic images or in silico diagrams of proteins from computer software, but have been utilised for a long time in ball-and-stick modelling kits. Even so, the potential colour holds for future uses in biology remains to be uncovered.

Elements began to be assigned colours in Corey and Pauling's colouring system. Koltun extended their ideas by continuing to categorise other biological molecules by colour, eventually personalised by modern molecular modelling software such as Jmol and RasMol. A clear inspiration is drawn from the appearance of pure elements; hydrogen, a colourless gas, assigned white, sulphur coloured bright yellow like its powdered form, chlorine aligned with its green gas, and bromine its dark red-brown liquid. Nevertheless, the link is harder to identify for oxygen and nitrogen, red and blue respectively. Potentially, oxygen is portrayed in its haemoglobin-bound form in the blood which has a striking red colour, whereas nitrogen is blue because it is the main component of the atmosphere that our eyes perceive as blue.

Colour seems to be widely adopted, but it can place some people at a disadvantage. Notably, colour blindness affects around 1 in 12 males and 1 in 200 females. Multiple sequence alignment (MSA) is a method that assesses the homology of protein sequences. To make biology more accessible to everyone, a new MSA shading technique has been developed to ensure inclusivity. The informative role of colour declines if colour-blind people cannot grasp its full benefit.

From a young age, we are taught a singular word that translates the wavelengths that our eyes receive. The various connotations associated with colour are also established: white as peaceful, yellow as happiness and red as dangerous. Therefore, it becomes second nature to connect colours with ideas.



This is extremely useful for quick analysis, but it could make us jump to conclusions too quickly as a result of the author's creativity or wanted effect. In short, colouring does simplify but labelling still helps to avoid any ambiguity.

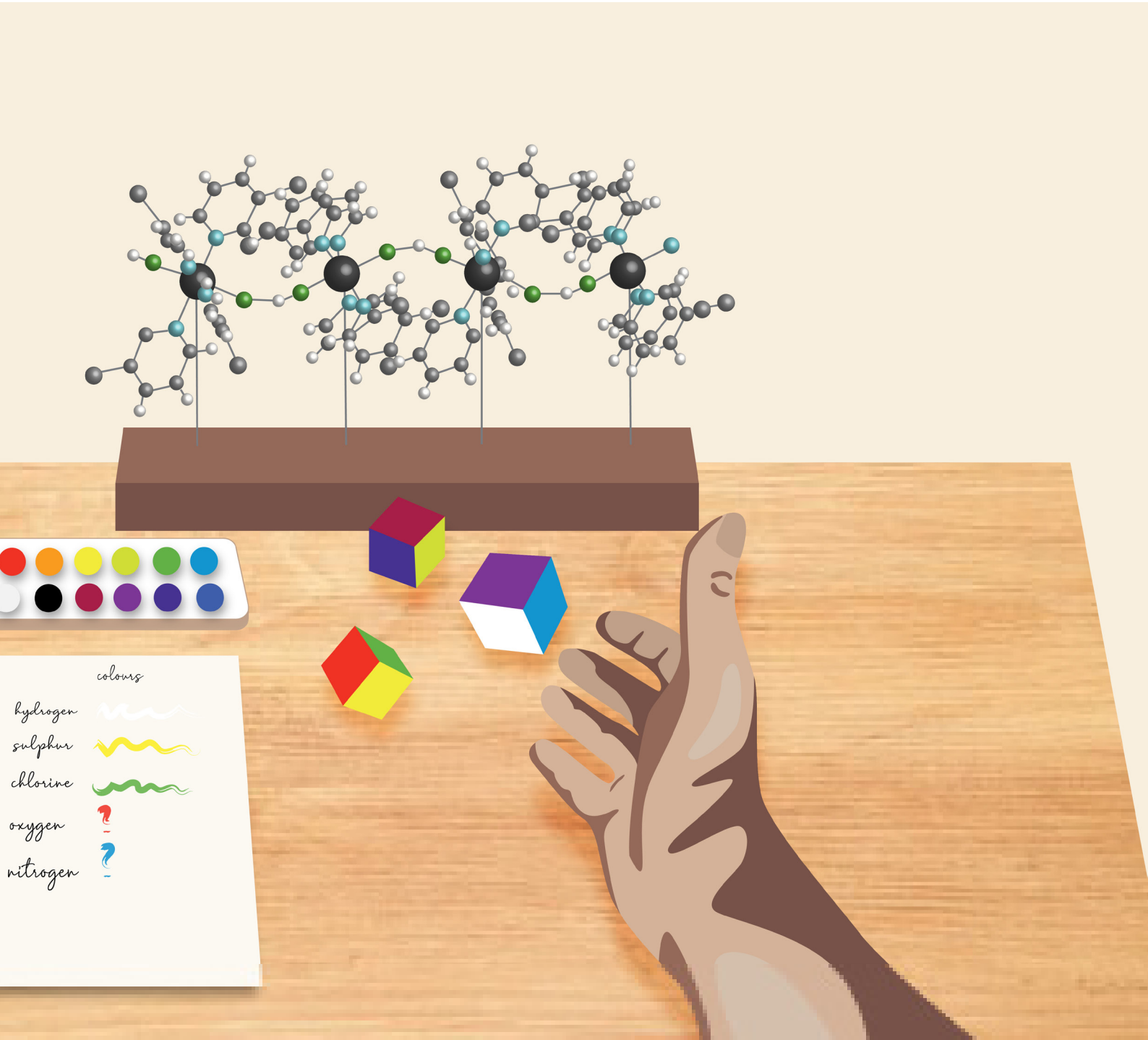
Biologists' applications of colour range from designing protein images, tracking messenger RNA in cells and producing fluorescent organisms. This immense output of data is exhilarating and eye-catching. The colouring system makes the invisible visible, but at times conveys slight deviations from reality.

Electron microscopy imaging does not reflect any colour, so why is SARS-CoV-2 known as a glowing red virus with crowned projections emanating from its membrane? Getting used to these types of images often causes mistakes in understanding that are overseen and left unnoticed. At the same time, it achieves the media's goal of alerting and persuading the population to take the pandemic seriously. To what extent can we then say that modifying scientific information might benefit the greater good?

If we base our perception of data solely on its physical appearance, the key message might be altered due to colours highlighting certain aspects while veiling others. The undoing of these misunderstandings can take time, but it might not even be necessary to get the main idea across.

The question remains: is filling in the lines of a biological colouring book a means to convey the truth behind scientific discoveries, or do complex ideas lose too much of their meaning through simplification?

Art by Rahel Kiss



Nature in Blue, Blue in Nature

The wonder of blue:
the rarity and complexity behind the colour.

Written by Sermila Ispartaligil
Art by Lucie Gourmet

Blue is everywhere, but is it really? The colour blue has a long history. Starting with azurite in the graves of Catalhoyuk (Turkey) in the sixth century, it extends to the genetically engineered chrysanthemums developed in 2017. However, the colour blue is quite rare in nature, and blue pigmentation is seldom seen in animals.

What appears as blue to the human eye is most often made possible by the ways in which animals and plants “perform tricks of the light to appear blue”, as Professor Andy Lowe describes it. This is explained by the difference between pigments and structural colour. Pigments are molecules that create colour by selectively absorbing and reflecting specific wavelengths of electromagnetic radiation. Structural colours, on the other hand, are the result of the shape and structure of a material instead of its chemical properties.

The appearance of the colour blue in nature is a wonderful example of the difference between pigments and structural colours. Structural colours can be classified according to the way that they scatter light: incoherent or coherent scattering. Incoherent light scatter occurs when individual light-scattering objects are randomly separated by a larger average distance than the wavelength. Conversely, coherent scattering of light is when the light-scattering elements are dispersed in an ordered way which prevents the phases of scattered light waves from being random. The light waves that are out of phase cancel each other, and waves that are in phase enhance each other. Some of the common examples of incoherent light scatter are blue sky, blue smoke, blue ice, and blue snow, while coherent scattering manifests as soap bubbles, iridescent oil slick on pavement, and the bright colours of insects and bird feathers.

The blue morpho butterfly is an example of the phenomenon of structural colours. It gets its colour from its wing scales that are shaped in ridges which bend light so that only blue wavelengths are reflected. Another explanation is that the nanostructures of their scales cancel all wavelengths except for blue ones, by the unique way in which they reflect light. Measurements from a paper by the Royal Society show that some morpho butterflies’ wing microstructures reflect up to 75% of the incident blue light. Lowe also suggests that the feathers of blue birds get their colour by their microscopic beads which are ordered in a manner that lets every wavelength of light be cancelled out except for blue. However, there is one exception to blue pigmentation in animals. The obrina olivewing butterfly is often cited as the only known animal to produce a true blue pigment.

When it comes to plants, they produce the colour blue by mixing their palette of pigments. Anthocyanins are prominent pigments that appear red at acidic pH and deepen into blue and purple hues with increasing alkalinity. These changes, together with reflected light, help create such flowers as plumbago, cornflowers, bluebells, and dayflowers. As Beverley Glover, a botanist at Cambridge explained, “Flowers are doing crazy chemistry to generate that blue.”

On the other hand, the reason why blue leaves only exist on the floor of tropical rainforests relates to the physics of light. The apparent colours result from the wavelengths of light that are reflected, not absorbed, by the pigments. Green chlorophyll doesn’t absorb, but reflects green light. Given that blue light has the highest energy in the visible spectrum, it is very rarely reflected by plants. The pigments of plants include chlorophylls, which give the green colour to leaves; carotenoids which produce orange (carrots), red (tomatoes), and yellow (maize); betalains that create the red colour of beetroot; and anthocyanins.

So why do these animals and plants have such complex structures to obtain blue in all these challenging ways? The answers are reproduction and survival. The various colours of plants can attract pollinators, while animals might use it by either attracting mates or warning predators such as the poison dart frog.

Thus, even though blue is highly prominent in our lives, it is not as prominent as we may think in nature. It is not as simply created or frequently found as it might seem. What appears as a simple blue pigment to us might be an ingenious play of light instead. Therefore, blue is not everywhere, at least not in the most apparent and simple sense of the word. Wherever it is, it is there to make us wonder.

THE GALÁPAGOS ISLANDS: THE BIRTH OF ITS BIODIVERSITY AND THE IMPORTANCE OF ITS CONSERVATION

A 2021 breakthrough study has uncovered the key to life in one of the most biodiverse places on the planet, and why it needs to be protected, now more than ever.

Written by Ericka Mejía Farias Art by Lucie Gourmet

Biodiversity, or the biological variety of life on Earth, is important for the sustainability of all organisms on the planet, including humans. According to Conservation International, there are only 36 key biodiversity hotspots on the planet, and while these hotspots cover only 2.4% of Earth's land, they account for around 60% of all its animal species.

The South American country of Ecuador is known to be one of the most biodiverse places on Earth, and is home to the Galápagos Islands. These volcanic islands are 1,000 km off the Ecuadorian mainland and are known to have a harsh, dry, inhospitable environment. And yet, the Galápagos are classified as a biodiversity hotspot. This strange paradox has stumped scientists for centuries, until now.

A 2021 breakthrough study by the UK National Oceanography Centre and the Galápagos Science centre used a high-resolution computer model of ocean circulation around the Galápagos archipelago to finally uncover the secret to its unprecedented biological success: wind. More concretely, the presence of nutrient-rich algae that comes from a cold-water upwelling in the surrounding ocean caused by key seasonal winds.

The study discovered that northward-flowing winds along the meridian facilitate

mixing of the upper layers of the ocean in the Galápagos region. This wind-driven upwelling of water allows the colder, nutrient-rich deep ocean water to rise and displace the warmer nutrient-deficient surface water, increasing nutrient supply for the phytoplankton, or algae, located in the light-receiving top ocean layers.

This critical upwelling occurs primarily along the western coast of the Galápagos archipelago, particularly during dry seasons. The study found that the shape and location of the Galápagos islands are crucial for these wind-ocean interactions; by blocking the westward-flowing south equatorial ocean current, the western coasts create density fronts that predispose the area to wind-driven upwelling. Moreover, the northward winds are responsible for driving the Humboldt current, which brings cold Antarctic waters to displace the warmer waters in the region.

The phytoplankton that benefit from this upwelling are a key food source for many of the animals found in and around the Galápagos. The presence of this algae is believed to have led to the migration of many land and marine animals to the Islands from the Ecuadorian mainland and surrounding ocean. Algae served as the main food source for krill, which were eaten by sea birds that flew from mainland Ecuador. Krill-eating iguanas and other reptiles arrived in style by sailing on floating logs, whilst penguins from Antarctica and Argentina likely took the Humboldt current. Marine animals came from nearby waters, drawn by the abundance of algae-eating fish and crustaceans.

Furthermore, the harsh conditions of the Islands have caused many of these land and sea animals to adapt through natural selection, further diversifying the animal population. Hence, this western area of seasonal wind-driven upwelling is heavily responsible for the creation and maintenance of one of the most biodiverse places on the planet.

So why does this matter? The Galápagos are one of the largest UNESCO World Heritage Sites on the planet and have the highest levels of endemism on the globe, meaning that the majority of its local species cannot be found anywhere else in the world. These animals are at an acute risk of extinction, which would result in irreplaceable losses to our planet; indeed this was sadly the case with the last Pinta Island tortoise, the late Lonesome George. So, understanding the wind and ocean forces that maintain this biodiversity is crucial for improving conservation efforts.

Unfortunately, industrial fishing fleets have also exploited this seasonal phenomenon and currently focus their fishing activities in this area of upwelling. Overfishing is one of many threats to the wonderful biodiversity of the Galápagos Islands along with pollution, human colonisation, the introduction of invasive animal species, and climate change. Climate change in particular has caused an increase in El Niño phenomena, which decrease density fronts and result in weaker winds in the area; this directly reverses the Galápagos upwelling, increasing water temperatures and depleting algae populations, thereby killing off many endemic species.

Conservation of these islands is essential, which is why there have been calls on Ecuador's current president to expand the Galápagos marine reserve, in order to protect more species from industrial fishing. There are also global initiatives to slow global warming, which has been negatively impacting the cold upwellings needed for the survival of the Galápagos.

Now, more than ever, we need to come together to harness this new scientific knowledge to help conserve such an invaluable piece of biodiversity, because, in the words of Sir David Attenborough, "if we take care of nature, nature will take care of us".

VOLCANIC ASH: A POSSIBLE ALLY IN THE FIGHT AGAINST CLIMATE CHANGE

Technological solutions to mitigate climate change often discuss renewable energy or carbon capture and storage. But what about volcanic ash?

Written by Chelsea Tripp Art by Patrick Marenda

Soaring temperatures, fluctuations in rainfall, and rising gas emissions. These are some of the issues exacerbated by climate change, and do not cast a positive outlook for dealing with what the Lancet has described as the "biggest health threat facing the world". When thinking about climate change solutions, we envision a more eco-aware world. A population that cycles more, abandons red meat for trendy vegan alternatives, and proudly displays shiny solar panels on the roofs of their homes. These lifestyle changes emphasise the consumer's responsibility to help slow down climate change, but until enough individuals can make these changes, alternative techniques are worth investigating. One innovative technology being considered is the distribution of volcanic ash into the oceans, storing carbon dioxide. So, how does volcanic ash present a unique solution to the challenge of climate change, rather than displacing the burden upon the individual?

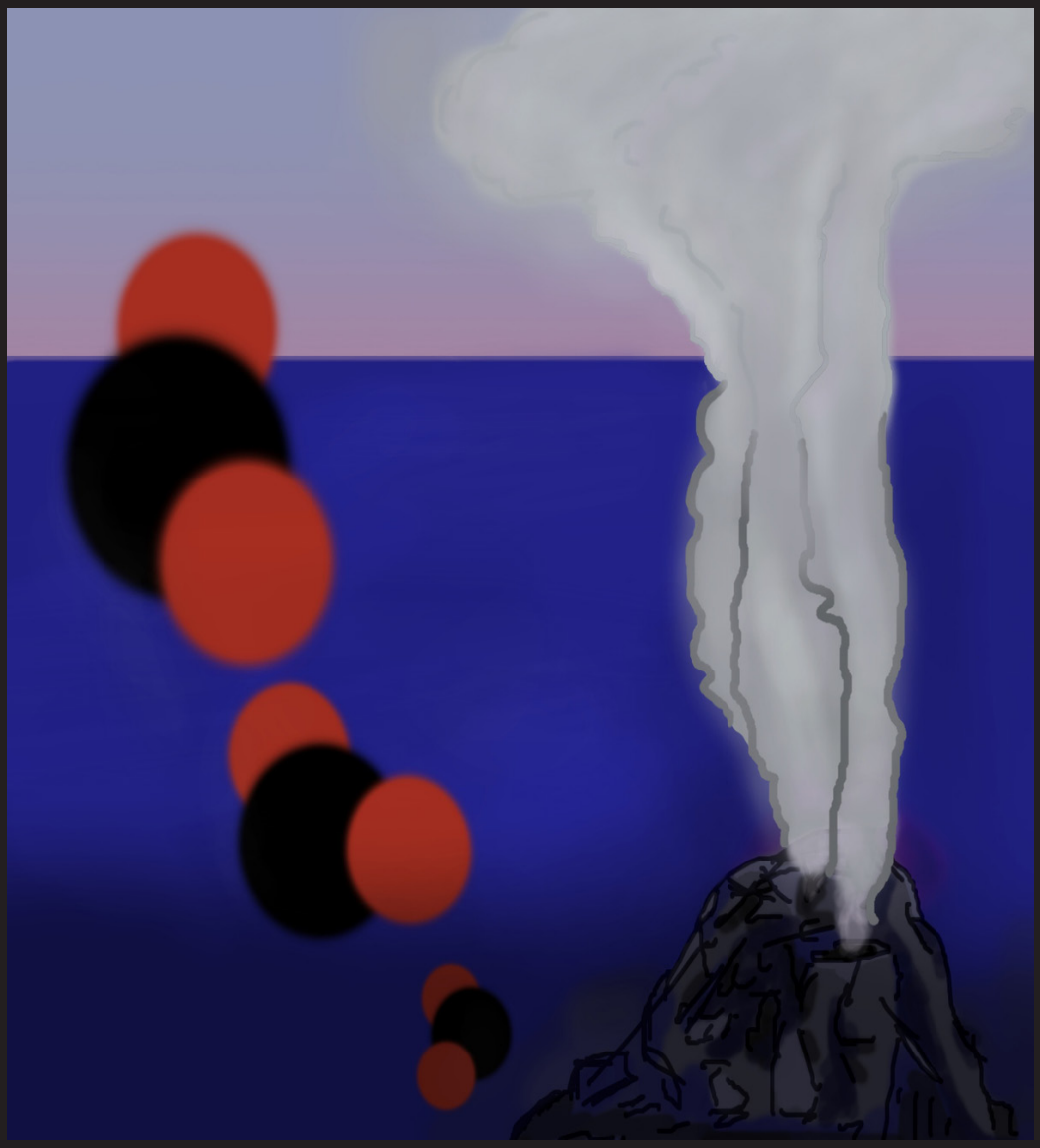
Volcanoes are commonly found close to or underneath the water. According to the US Geological Survey, 75% of approximately 1,500 active volcanoes worldwide are based near the Pacific Ocean, an area nicknamed the 'Ring of Fire'. However, volcanoes are paradoxical, as they can either help or hinder climate change. During an eruption, they produce sulfur dioxide particles. When merged with water, these particles reflect energy from the sun, thereby promoting cooling. They also generate carbon dioxide, a greenhouse gas notoriously known for its contribution to the planet's global heating.

A more unusual method to remove atmospheric carbon dioxide is through the artificial placement of volcanic ash in our oceans. Following a volcanic eruption, ash, or tephra, is naturally produced and deposited on the ocean floor. Whether naturally produced or synthetically placed, the knock-on effect of these ash deposits serve to lock away carbon for hundreds and potentially thousands of years. As such, tephra is a crucial climate change solution, acting as the ocean's very own carbon storage units. As carbon sinks, the ocean also entraps more carbon from the air than will be released, absorbing around one third of carbon dioxide emissions worldwide. However, the effectiveness and safety of using volcanic ash in the fight against climate change is still uncertain.

Researchers suggest that for every 50,000 tonnes of extra volcanic ash placed into the ocean, nearly 2,750 tonnes of carbon dioxide could be stored by the seabed, at only £40 per tonne of carbon dioxide removed. Compared to other greenhouse gas removal techniques, such as carbon capture and storage, which transforms carbon dioxide into its liquid form before storing it underground, volcanic ash is relatively cost-effective as it does not require the same expensive technology. Earlier evidence from the 2008 volcanic eruption in the Aleutian Islands, Alaska, suggests

that marine algae benefit from the iron present within volcanic ash, as this nutrient aids their growth. Although this method builds upon a naturally occurring process, there are concerns that an excess of volcanic ash for prolonged periods could disrupt the delicate balance of our oceans, and impact how well they store carbon. It is also possible that a heavy flow of ash spanning a large area could negatively impact the ocean's pH or affect certain coral species due to the excess iron and magnesium.

Artificially placed volcanic ash within our oceans has the potential to store large amounts of carbon dioxide, at much lower costs without the need for complex technology, and with further research, could have additional benefits for marine life. But for this technique to be successful, we cannot solely rely on technological innovation to rescue us from an anthropogenic problem. The UK plans to cut carbon dioxide emissions by 68% in 2030, and a united effort from science, technology, leaders, ordinary individuals, among other societal sectors, is fundamental to reaching these targets.



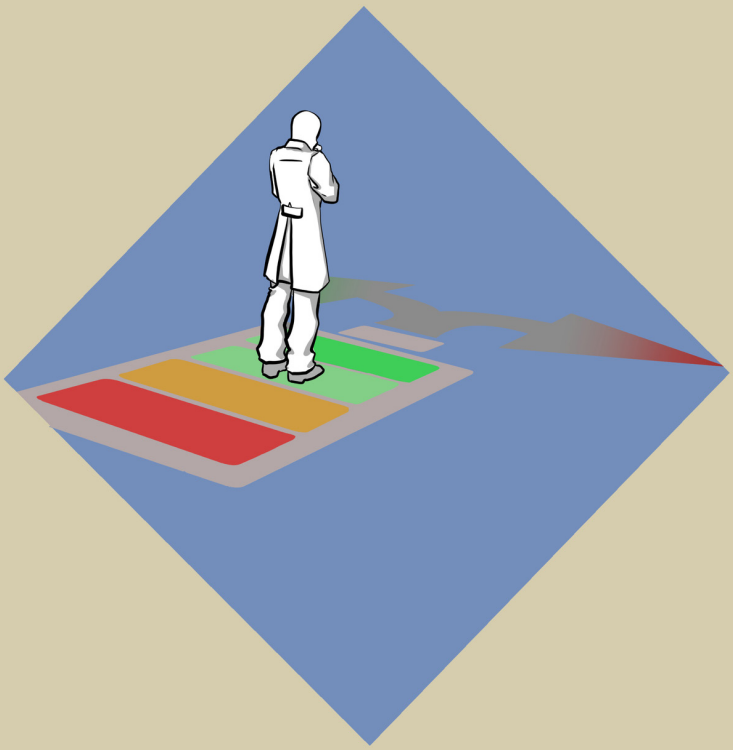
LITHIUM-ION BATTERIES: WILL THEY DRIVE US TOWARD A CLEAN FUTURE?

Quick to praise electric vehicles, many are unaware about the grim realities laced in their crucial components.

Written by Maria Stoica Art by Doheon Kim

Sleek and bold, Teslas have become emblematic of what electric vehicles (EVs) have the potential to be. But what their seductive exteriors hide is something more complex – lithium-ion batteries. A conservative model predicts an increase of 3000% in global electric vehicle stock by 2030, a figure which is further bolstered by countries such as Norway banning the sale of petrol and diesel cars by 2025. Therefore, lithium-ion batteries will be critical in a move toward 'clean' transportation.

But lithium-ion batteries pose significant issues that we must reckon with – sooner rather than later. One of these is that battery technology is not progressing in accordance with growing demand, worrying scientists. However, the ethical quandaries coiled in lithium-ion batteries are more pressing. We need to contend with the contradiction that arises when we glorify EVs as a central solution to climate change yet fail to consider the problematic supply chain behind their batteries.



The supply chain of lithium-ion batteries begins with mineral extraction, often synonymous with unethical practices. As their name implies, lithium-ion batteries rely on a large amount of lithium, lauded as 'white gold'. Home to 54% of the world's revered resource and a favourable business environment, the salt flats of South America's Lithium Triangle are the backdrop to most lithium mining. Crucial to lithium mining is water extraction, which has reached such a devastating level that it prevents local communities from accessing water to meet their basic needs. To illustrate the horrors of this reality, mining activities have used 65% of water in Chile's Salar de Atacama region. The ability to harvest food and provide nourishment for animals – two major types of livelihood – is significantly dampened. In short, with demand for lithium rising, water shortages might prove deadly to local communities.

Most worryingly, that prediction fails to account for the possibility that the supply of lithium will be depleted by 2025, which would only leave communities in a lurch. The lack of support afforded to communities is also reflected in the alarming fact that only one in five lithium producers has integrated a human rights policy in their mining activities. Even scientists working on battery technology have called attention to the issue of most producers regarding cutting corners as the status quo. Therefore, there is a need to overhaul the regulatory framework that currently enables producers to operate with such appalling governance. Otherwise, can lithium-ion batteries truly be hailed as the 'key' to the green revolution? Lithium extraction does not occur in a bubble of its own, and it is a disservice to pretend that it does.

Communities local to South America's Lithium Triangle are not the only ones impacted by mineral extraction. Although 6,000 miles apart, the grim horrors of lithium extraction are familiar to cobalt miners in DR Congo. Cobalt is similarly important to the production of lithium-ion batteries and, for the most part, found in DR Congo. An investigation into cobalt mining practices led slavery expert Siddharth Kara to estimate that of the 255,000 cobalt miners in DR Congo, at least 35,000 are children, some as young as six years old. Even the coolness of the tunnels where cobalt miners spend the majority of the day cannot offer respite – death always lingers overhead.

Child cobalt miners have died as a result of tunnels collapsing on them. Enough of such tragedies have occurred for a lawsuit to be waged against Tesla and other tech companies for their failure to choose ethical cobalt producers. Lithium-ion batteries are tainted with the blood of child labour. As Western countries push for EVs at an unabated pace, the demand for cobalt will only increase unless structural change is implemented. For one, companies such as Tesla must hold their producers accountable, as realistically, that's the only source of pressure they would respond to.

Companies are cognizant of the ethical implications that underpin mining. A small glimmer of hope has come from the increasing pressure to improve lithium-ion batteries: Panasonic claims it will commercialise a cobalt-free version of battery cells it supplies to Tesla within the next two to three years. While perhaps the most recognisable, Teslas are not the only EVs on the market, meaning this technology must become the new standard for it to fulfill its potential.

When Tesla calls for a "zero-emission future" then, it's accessible to only a fraction of the world. Right now, a zero-emission future is costing local communities their livelihoods and children. Too many ethical issues plague the mining of lithium and cobalt for them to be a viable component of batteries in EVs going forward. Battery technology can be improved – it's solely a matter of time. But until then, in failing to acknowledge the hypocrisy that underpins such ventures, we perpetuate an injustice that impacts millions.

Conservation:
Are we prioritising marketable animals?

WHY ARE YOU MORE LIKELY TO MAKE A DONATION TO HELP PANDA BEI BEI THAN TO SAVE A SANDWORM POPULATION?

Writer and Artist: Patrick Marenda

Not every species can be saved. This is a sad reality of conservation, which raises the question: who should be saved? And what can we afford to lose? How can we categorise between the two? Are we as humans not taking too much control in giving ourselves the right to choose what animals to save and which to let die? This becomes then not just an ecological but a deeply ethical question.

Let's take a look at the wildlife page of the WWF. Out of 18 entries, only 3 are non-mammals (the sea turtle, the emperor penguin and the adelie penguin), and not a single invertebrate is in sight. Our anthropocentrism hides the majority of life's diversity and leads us to prioritise animals which are similar to us, meaning vertebrates and specifically mammals. This is especially true if they are cute, furry and are present in children books, zoo promotions and souvenir shops. A wonderful illustration is the logo of the WWF, in which a giant panda is promoting the safeguarding of worldwide wildlife.

The promotion of a few dozen highly popular, mostly mammalian and almost exclusively vertebrate animals may mislead us to underestimate the number and diversity of global wildlife. On the other hand, it seems true that most people are more willing to donate to save charismatic and human-like species such as apes or lions. One can think here of the 'Big Five' in South Africa, which are the ones that attract tourists, visitors and with them financial benefits. As humans, we are more likely to have compassion with a named individual than with a whole species or even an ecosystem.

This bias starts in childhood, indeed many children will prefer cute or strong animals over their small, un-charismatic counterparts. In an effort to raise support for such species, like mussels, outreach specialists often try to make them appealing through comics and stories in which those animals become superheroes with their own superpowers. When people know and like a character, they can muster enthusiasm for the species it represents in the real world, which they would have previously ignored at best.

It is often said that the protection of more popular animals can contribute to saving other less well-known species sharing their habitat. While it is likely that by protecting rhinoceroses who need a very large area, one also helps to protect other less iconic species, this isn't always true. For example, the establishment of panda sanctuaries in the mountains of west Sichuan has also helped to save many other species in this landscape, but some species such as leopard, snow leopard, wolf and asian wild dog have almost disappeared. While snow leopards can still raise money on their own, other species do not have this

Indeed for such charisma-challenged species, conservation projects are often led by smaller organisations. Zoos are also a crucial actor, as they often offer shelter and love to these lesser-known animals, and the people working for zoo administrations are keen to help in the conservation effort.

Prioritising the conservation effort on highly diverse and unique ecosystems, and within them keystone and umbrella species, is a step towards maximising the amount of biodiversity saved. Indeed with dangers such as massive deforestation and wildfires progressively eroding habitats, it is even more important to prioritise the safeguarding of the biodiversity of our Earth. In this perspective, focusing on biodiversity hotspots could help to protect 35% of all vertebrate species, conserving 1.4% of the Earth surface. These biodiversity hotspots contain a remarkably high concentration of biodiversity with many unique species. It remains to be seen where finances should be deployed in order to have the best chances of saving the most biodiversity. Scientist Hugh Possingham has developed an algorithm which tries to calculate the best trade-off, measuring real-world costs against the number of species saved. While improving year by year, it is still difficult to put numbers on many factors implicated in the success of a conservation campaign.

This should be the place where I tell you that while the future may look pretty bad, we can save the world through our good intentions and the power of friendship. But this type of ending does not seem fitting anymore. Although biodiversity is dying away, hopefully we can save a certain amount of it, if we are careful and smart about it. So, I hope that after reading this you are not too discouraged and still want to help save Earth's biodiversity, be it through donating to large non-governmental organisations and their cast of superstars, or maybe to a smaller initiative or a zoo, in the protection and conservation of a lesser-known species.

The uncomfortable truths of pet ownership

Our obsession with cats and dogs is killing billions of animals every year.

Written by George Blake Art by Stephanie Chang

As lockdowns were implemented across the world last spring, there was a sudden surge in demand for pets (mainly cats and dogs), as loneliness pushed people towards acquiring an animal companion. The Pet Food Manufacturers' Association found that 11% of all UK households acquired a new pet during lockdown, and in London this figure was as high as 18%. Puppies sold on pets4home, Britain's largest online advertising site for pets, have doubled since before the lockdown, with many puppies now costing thousands of pounds.

Pets have no doubt helped their owners to cope better emotionally during the lockdown, but the cause of these benefits and the broader mental health implications of pet ownership are still debated.

Is the conversation surrounding pet ownership flawed? Should we view and think about pet ownership solely from a self-centred perspective, or do we need to consider their wellbeing too? And something many of us might not think much about: what about the environmental impacts?

Although still niche, the environmental cost of pets is the subject of increasing research, and the results are rather harrowing.

Pet owners are likely familiar with the sight of their beloved canine or feline friend bringing home a dead rabbit or bird, nature's prize kill, but the sheer scale of the ecological costs of pets may come as a surprise. In the UK, pet cats are estimated to kill at least 275 million animals annually, the majority of which are native species, while a study in the USA determined that free-ranging domestic cats (both pets and feral) are the single greatest source of anthropogenic mortality for birds and mammals. The study estimated that between 7.6 and 26.3 billion birds and mammals are killed annually, and roughly a third of these are due to pet cats. Overall, cats have proven themselves worthy predators, driving 63 species to extinction (40 birds, 21 mammals, and 2 reptiles).

Dogs are not that much better; they constitute the third worst human introduced predator, just behind cats and rodents, and have led to the extinction of 11 species. Today, they threaten close to 200 species, 30 of which are critically endangered, 71 endangered, and 87 vulnerable under the IUCN red list.

While a common response to these concerns may sound something like "my dog/ cat would never kill anything, so surely I can still let them outside?", this fails to acknowledge that the mere presence of domestic pets can alter the behaviour of 'native species', resulting in sub-lethal effects. The presence of dogs can reduce the parental care of adult birds towards their young, drive deleterious effects on the breeding success of ungulates, and even brief appearances of cats can lead to increased egg and young bird predation by third party animals.

A further concern is that diseases can be spread via domestic animals. Remember that brief period when we all feared our pets were spreading COVID-19? Well, dogs actually do act as vehicles for the spread of rabies and canine distemper virus, repeated outbreaks of which have occurred in endangered Ethiopian wolves and even led to population declines of the threatened Lake Baikal seal. Cats meanwhile spread a pathogen known as Toxoplasma gondii, which only occurs in the intestine of felines. Infected cats excrete the pathogen, which then moves like plastic or pesticides into waterways and often results in the deaths of iconic marine mammals, such as beluga whales or California sea otters.

Many still resolutely feel it is their right to allow their pets to roam freely, but the academics at the centre of many of the aforementioned studies say this must change. If they had things their way, there'd be no more kicking open the door to let your cat roam unsupervised, and no more letting your dog run freely along the beach or through the woods.

However, a clamp down on the freedoms pets currently enjoy raises serious issues itself. What quality of life would we be providing our pets with were we to follow these instructions? Keeping them trapped inside or solely walking them on leads would reduce mental enrichment and would arguably take way from the joy of pet ownership. A possible compromise could be to exclude pets from any ecologically sensitive areas, although such exclusions would need to be legislated for and must follow the precautionary principle: if the importance/ sensitivity of a habitat is unknown, pets must be excluded.

The situation is further complicated when one considers the carbon footprint of pets. Cats and dogs are primarily carnivorous, and although there is growing demand for vegan pet food, most cats and dogs still consume large amounts of meat. Professor Gregory Okin, a member of UCLA's Institute of the Environment and Sustainability, found the USA's 163 million cats and dogs accounted for 25-30% of national meat consumption. If these cats and dogs constituted a country, the nation would rank 5th in global meat consumption. When combined with the faecal matter they produce, pets in the USA produce 64 million tonnes of greenhouse gases annually, roughly equivalent to Austria's total annual emissions. To reduce the carbon costs of pet food, there needs to be a commitment to using all parts of animal meat, so-called snout-to-tail consumption, but in reality, there is a growing trend towards premium pet food, which often contain cuts that would be suitable for human consumption.

The carbon footprint and direct impacts on native wildlife of domestic pets provides a strong argument for a fundamental shift in the way we care for them. Although for some, like Pete Marra the author of Cat Wars: The Devastating Consequences of a Cuddly Killer, this does not go far enough. He has called for a cull of feral domestic animals, which may seem abhorrent to many, but really this depends on whether you believe it is right to prioritise native species over feral animals. At the very least, it seems there is a decent argument for a dramatic increase in funding towards sterilisation services of feral animals.

The ecological and environmental costs of pet ownership are considerable and diverse, and it is essential we begin to take these issues seriously. Some may argue it is time to start rethinking the habit of owning pets entirely, particularly given that global pet ownership is projected to rise even further in the coming decades.

But, solely looking at the cold hard facts and statistics of pet ownership overlooks the numerous small joys they bring to us everyday, and quantifying their benefits towards our mental health is far more challenging than determining an ecological footprint.
Therefore, this piece is not advocating that people shouldn't have pets, only stressing that there are measures we can all take. If you do decide to get a pet, perhaps stick to just one, and look to adopt rather than buy. Over 100,000 dogs and cats are without homes at any given time, and roughly 20,000 dogs in shelters are euthanised each year.

Most importantly, this piece is bringing to the forefront that the compassion and love we give our pets should be extended to all species. Our pets are not unique and all animals are complex, fascinating, and amazing. Perhaps it's time we started treating them all as equals.

Is it too late to turn the tide on water scarcity?

In 2018, Cape Town nearly ran out of water. How can we make sure history doesn't repeat itself?

Written by Alexander Hancock Art by Sophie Maho Chan

Under the stifling heat of the sun, residents of Cape Town line up to collect their daily water rations which have fallen to 13 gallons each. Holding large jerricans and empty containers, the city dwellers flock to the natural springs which are patrolled every hour of the day by police who stand guard, ready to quell any tussles or disruptions. After years of droughts and poor city planning, Theewaterskloof dam - which accounts for half of the city's water supply - is drying out. Residents have no choice but to cut down their daily water usage and hope for rainfall. Until then, 'Day Zero' - the point at which the government will cut most of the water supply to homes and businesses around the city - looms closer. Daily rations will drop to roughly six gallons.

Water scarcity affects roughly 2.7 billion people around the world, and refers to the shortage of freshwater supplies that are needed to provide and sustain a specific area. Dwindling freshwater resources are caused predominantly by climate change, food production and population growth. As reservoirs dry up and rivers accumulate waste, poor access to freshwater could affect two thirds of the population by 2025.

The implications of water stress are far-reaching and could cause millions of people around the world to suffer from dehydration and waterborne diseases contracted from unsafe drinking water like cholera. Not only has water scarcity brought on a health crisis, its calamitous effects on the environment, economy and political relations could have

profound ramifications for global peace. Geopolitical tensions between Ethiopia and Egypt surfaced after the Ethiopian Government revealed plans to construct the Grand Renaissance Dam on the River Nile, a project aimed to provide Ethiopia with hydroelectric energy. The Egyptian Government believes the dam will slow down the flow of the Nile to Egypt which is the source of 85% of the country's water supply. Many fear this row could lead to future wars.

The environmental, health, economic and political implications of water scarcity show no signs of slowing down. So how can governments mitigate the alarming risks of water shortage around the world, whilst global temperatures soar and population figures rise?

One solution to mitigating declining water supplies is by improving irrigation efficiency. With 60% of the planet's freshwater used for irrigated farming, strategies that reduce the amount of water used in agriculture whilst yielding optimal crop rates have been developed to alleviate the water crisis. From swapping overhead irrigation systems with drip irrigation systems, to ensuring that leaks and punctures in irrigation equipment are frequently supervised, logistical changes to farming practices could have profound global impacts on water conservation.

Another promising solution to water scarcity is the use of desalination technologies. Desalination involves the removal of dissolved salt from water, which renders ocean water safe for human consumption. Countries with arid climates like Saudi Arabia rely heavily on this process to combat their depleting freshwater supplies. The two main approaches to removing salt from otherwise non-drinkable water are thermal desalination and reverse osmosis which involve vaporising and condensing salt water, and purifying brackish water using permeable membranes to trap salt. While the process of removing dissolved salts from saline water is a costly endeavour which often requires large amounts of fossil fuel-based energy, recent innovations including solar-powered desalination units could help to rectify these issues. Cost-effective and eco friendly, the newly developed solar-powered system could supply upwards of 1.5 gallons of fresh drinking water per hour for every square meter of solar collecting area according to the Massachusetts Institute of Technology.

Yet for all of the benefits of improving irrigation efficiency and using solar-powered desalination units, both processes are inherently flawed. Evidence suggests that altering irrigation patterns negatively affects groundwater recharge; the process by which water trickles through soil to refill aquifers. And desalination technologies, whilst providing fresh water to millions around the world, pump the resulting brine and chemicals that build up during reverse osmosis back into the ocean, which can disturb aquatic ecosystems and pollute waters.

Fortunately, 'Day Zero' has thus far been avoided, thanks in large part to the introduction of strict curbs on water use during 2017 which included fines for watering plants and filling pools. The long-awaited arrival of rainfall and a shared mentality to preserve the valuable resource were just as crucial in delaying the feared day. While other countries look to hidden water supplies and technological breakthroughs to combat water shortages, it is arguably the act of looking inwards at society's careless use of water that will solve the shrinking supply of the precious resource. In England, people use an average of 36 gallons of water each day. According to the head of the Environment Agency, Sir James Bevan, the country's overconsumption of the resource could lead to water shortages in the next 25 years. While many have called on the government to establish water pathways between areas with vast supplies of water to areas with low supplies, the majority argues that the fight against the water crisis begins at the micro level. Waterwise, the UK-based NGO, suggests that in order to delay England's water crisis, the country's daily water usage would have to drop to 26 gallons. By installing water efficient toilets, using low flow shower heads, and buying second-hand clothing, daily water usage could fall dramatically.

Perhaps until water-secure areas - like the UK - are faced with the harrowing fear of living off a drastically reduced water supply, will there be any real changes to this impending crisis.

The Price of Health

Brexit reforms may threaten medical innovation.

Written by Jenny Katsouli Art by Sophie Maho Chan

What is the medical research budget – and why should we care? A tiny fraction of the taxes we pay each year is channelled towards publicly funded institutions such as universities, multi-centre clinical trials and research institutes. So, you can pat yourself on the back for having some part in funding the Oxford COVID-19 vaccine and that promising new cancer nanotechnology therapy featured on the news.

Understandably, scientists are dreading a potential medical budget cut that may accompany the inevitable reforms that a finalised Brexit would introduce. Research institutions, such as universities, have multiple revenue streams for research. However, governmental funds are often the most substantial. Cutting down governmental support of medical research is like cutting the blood supply to the heart.

Globally, a third of all new approved medicines originate from publicly funded institutions. In the US alone, the 210 new medicines approved during 2010-2016 all benefited directly or indirectly from publicly funded research. When the public invests in research via taxes, better therapies and diagnostics become available and accessible. For example, the PROUD clinical trial, which aimed to test the efficacy of the drug Truvada-PrEP, was financially supported by the MRC Clinical Trials Unit at UCL and Public Health England. The trial demonstrated a 86% reduction in HIV infection in the participants using the drug. Because of these remarkable results, the drug is expected to drastically minimise expenses for the National Health Service (NHS), since each HIV patient faces disease-related costs upwards of 300,000 pounds during their lifetime.

As well as supporting research in universities, public funding drives innovation based-economic growth in research institutes. For example, the Dementia Research Institute strives to tackle the booming burden of dementia, which is expected to affect one million UK citizens by 2020 and cost the NHS more than 1 trillion pounds over the next four decades. As health activist Mary Lasker cleverly stated, "If you think research is expensive, try disease."

As publicly funded medical research is a massive undertaking, it is unlikely to be replaced by private initiative. Pharmaceutical companies closing down their research and development (R&D) facilities has become part of a wider global trend. Nine years ago, Pfizer closed down its largest UK R&D site in Kent, which employed 2,400 people. The company's spokesman Andrew Widger stated: "Like all of our industry peers, Pfizer is challenged with insufficient productivity and an unsustainable model for innovation." Since then, many companies have followed Pfizer's example. Most recently, Eli Lilly announced the closure of the Erl Wood research centre in Surrey, which had been operating for more than 50 years.

Multinational companies that have decided to shut their innovation facilities are driven by financial considerations. Drug development ranges from 870 million to 1.9 billion pounds and takes up to 12 years to complete. However, less than 12% of potential drugs that start Phase I trials will receive approval and launch on the market. Most for-profit corporations cannot bear such costs. Hence, publicly funded institutions often carry out preclinical research, which is then sold as intellectual property or entrepreneurial collaboration to pharmaceutical companies. This is considered a mutually beneficial transaction since they can reinvest their profits into research and innovation. A recent example is the AstraZeneca COVID-19 vaccine. University of Oxford, with taxpayer support, had been investigating a vaccine that could be readily developed during an outbreak, long before COVID-19 hit. In April 2020, AstraZeneca identified this innovative preclinical research and saw it through development, manufacturing and distribution. Overall, this demonstrates that it is essential that the public, who have the most to gain from medical research, funds the research that will improve their quality of life and mitigate the risk of disease.

Medical research brings tremendous value to our lives, both metaphorically and literally. Research shows that population health and longevity, which stem from medical research, bring increased productivity. A recent study estimates that for every 1 pound invested by the public in cancer and cardiovascular medical research, 27 pence will be returned in interest every year. In fact, a unit of measurement called QALY assigns a monetary value to the health gain and standard of life improvement that research brings. An example of such cost-saving medical research was conducted by the UCL group led by Professor Jayant Vaidya at Royal Free Hospital. In the course of 20 years, the team developed TARGIT IORT, an innovative radiation therapy for breast cancer. With this technology, women can skip the usual postoperative daily radiotherapy sessions, usually lasting 3-6 weeks, and can resume their lives immediately. TARGIT IORT therapy offers financial value as well; it is estimated to save the NHS 9 million pounds per year as patients take fewer trips to the hospital, patient management becomes easier and fewer radiation sessions must be prescribed.

In 2017, the UK invested 0.20% of its GDP in university research and development, ranking it 22nd worldwide in funding as a share of GDP. However, chancellor Rishi Sunak's new budget reforms, which are expected to be implemented within the next few years, may considerably shrink the budget allocated to medical research. The consequences of such a political decision would be alarming. The UK may lose its status as a global innovator and healthcare standards will decline as there will be little advancement in diagnostics, therapeutics and caregiving. As a consequence, the burden of disease, mortality and economic stagnation would grow. Ultimately, what seems to be a short-term national budget saving strategy will only result in long-term disease-related spending. Nevertheless, government officials may be pressured to reform their bills if the public intensely opposes them. Patient and public involvement has always empowered medical research. Expressing concern on social media, supporting research charities and signing petitions can make each one of us part of the conversation.

THE ETHICS OF MIND-READING

Can policy catch up with brain-computer interfaces, like Neuralink?

Written by Ebani Dhawan Art by Olivia Kehoe

I wrote this article without typing. No, not even with an old-fashioned pen and paper.

Okay, not really. But, it's not too distant a reality, thanks to brain-computer interfaces (BCIs).

You may have heard of BCIs in August 2020 when Elon Musk's Neuralink live-streamed their progress update. It stirred public conversation about incorporating BCIs into today's society. With potential to aid those unable to be independent, BCIs are seen as a way to enhance lives. However, this evolving neurotechnology blurs the fine line separating biology and technology, raising an important question amongst neuroethicists and regulators: will BCIs undermine what it means to be an autonomous human?

BCIs are computer-based systems that interact with the brain and central nervous system to record electrical signals produced by neural activity. This technology is either invasive, connecting directly to nerves via implanted electrodes, or non-invasive, such as electroencephalography-based systems that record signals from outside the skull. BCIs also can stimulate neural circuits in various cortical regions, controlling specific brain circuits.

As the range of potential applications of BCIs grows, so too does the pressure facing regulatory bodies. Although neurotechnology is in its infancy, these groups need to think about policy. Postponing this to when BCIs are socially entrenched would be too late. The need for legal clarity is imperative as neurotechnology is rapidly outpacing science policy, a typical relationship between law and science.

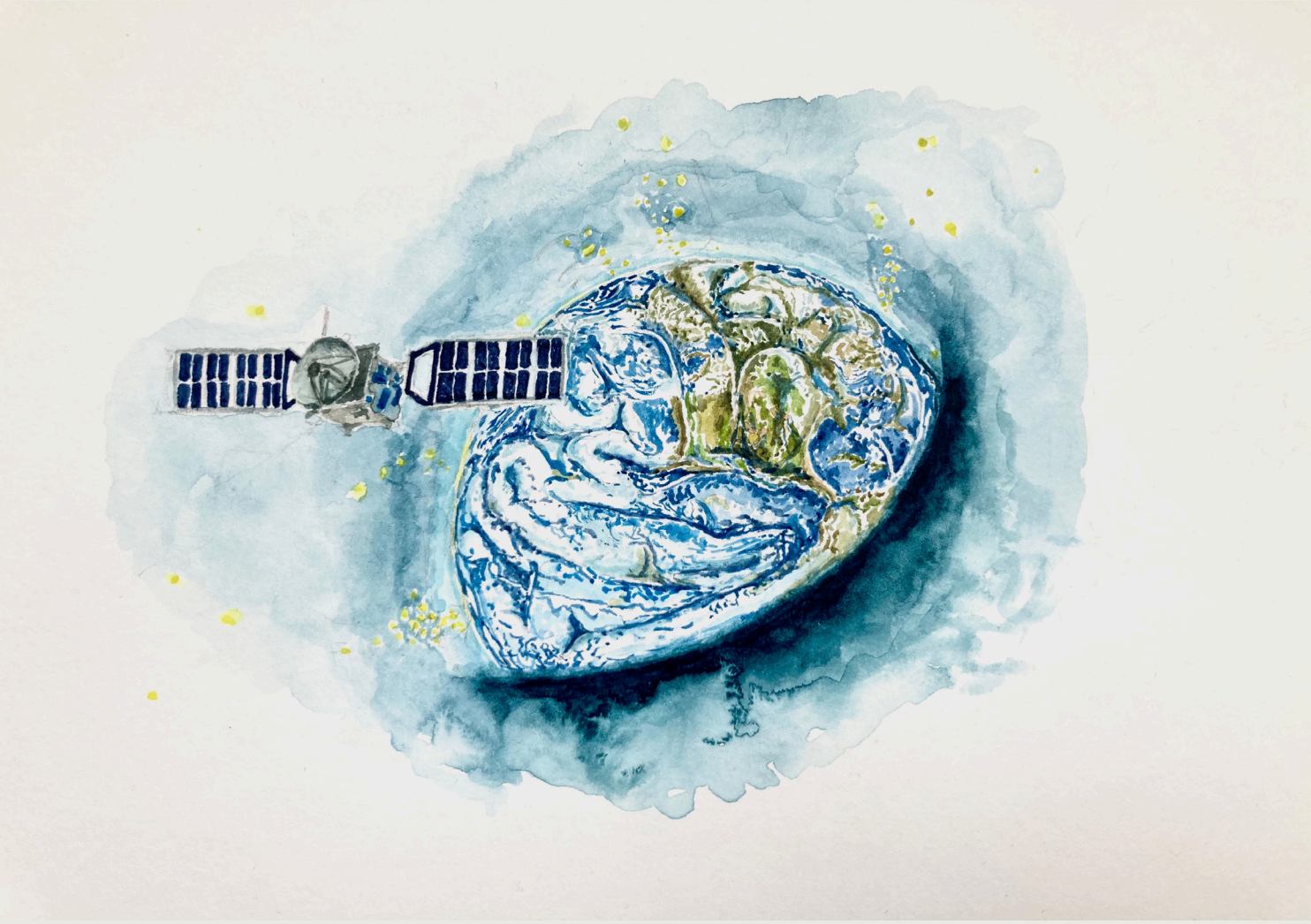
The major ethical issue policymakers will need to explore is the potential for BCIs to breach our sense of agency - the feeling that we are the primary cause of an action. Psychological evidence shows that this sense of control is dependent on sensory feedback, some sort of 'confirmation' that the committed action has had the expected consequences. However, there is a delay between the generation of brain activity and the output of the BCI, which diminishes the feeling of influence over an action. As a result, a diluted sense of agency can emerge.

This raises the regulatory question: who is accountable for the action? An altered sense of agency, whether it be diminished or shared, should mean altered consequences of accountability. BCIs present a possibility of technological external control over personal agency, which conflicts with the societal values of autonomy the legal system aims to protect. Western jurisprudence requires voluntary control (i.e. agency) to constitute legal liability. The majority of BCI-mediated actions are 'disembodied'; they do not require a bodily movement. So, legally, those BCI-mediated actions are not considered as actions because it does not fit with the notion of actus reus - an act needs to be committed for the individual to be liable. And, many common law codes consider an act to be committed with a bodily movement.

Turning to the effects of BCIs on an area closely entwined with our sense of agency - self-identity. Neuroimaging research highlights the medial prefrontal cortex and the medial posterior parietal cortex as the hubs of self-knowledge, knowing who we are. Acting autonomously means acting authentically, which can only occur when we are aware of our personal identity. BCIs can change this self-awareness. A 2019 study conducted by Frederic Gilbert at the University of Tasmania found that one participant transformed into a "new person" after an implantation of a BCI. Another, known as 'Patient 6', experienced a "radical symbiosis" with the BCI, so much so that losing it caused her deep grief, feeling as though she had lost herself. With such radical identity changes, which one is the true self? And, our old question pops up again: who is accountable?

Another significant ethical concern relates to privacy. Recent studies led by Martinovic and Rosenfeld have shown that using BCIs to override a user's privacy is not fiction. Sensitive information, such as debit card numbers, was successfully revealed through EEG recordings. Having access to one's brain signals can be seen as analogous to mind-reading. Although this may be empowering to certain users, such as those who have lost their brain-body connection, it exposes them to a new form of vulnerability. BCIs collect a vast amount of brain signals, some of our most intimate biodata. Our brain is the last refuge of personal freedom and self-determination, but BCIs threaten to publicise it. Losing the ability to keep information confidential undermines what it means to be a free society, a democracy and have human rights.

It is crucial that policy is proactive and precautionary when dealing with neurotechnology such as BCIs. Cognitively diverse expert groups and university and industry researchers require sufficient time to gather high quality evidence to back up the policy recommendations they make. With applications in medicine, user authentication, entertainment and smartphone technology, BCIs are humanity's next foray into transhumanism, blurring the lines between what is human and what is machine. BCI policymaking is still not a frequent point of discussion and it is imperative that society decides how to treat neurotechnology before it is too late.



The pill: A history that is hard to swallow

DRUG TRIALLING ON VULNERABLE COMMUNITIES HAS A EUGENIC PAST THAT LIVES ON TODAY.

Written by Lucas Heeringa Art by Lia Bote

The oral contraceptive tablet, colloquially known as 'the pill', has allowed countless people to take more autonomy over their lives and has rightly been heralded as one of the most impactful products of the 20th century. However, despite it being the most popular form of prescribed contraceptive in the UK, with just under 1 in 3 women using it, very few know the unsettling journey it took to get here. With COVID-19 vaccine trials covering the headlines this past year, it is important to understand the ethics of drug trials and how the populations chosen for them have historically been rooted in eugenics.

As it will soon become clear, it is fitting for the story of the pill to be intertwined with that of the oldest colony in the world; Puerto Rico. The Caribbean island's population of 3 million are all US citizens and have been since 1917. However, it is not an equal citizenship. Those on the island lack full voting power and have fewer regulatory laws protecting them. The latter is what made it so attractive to the American gynaecologist John Rock and biologist Gregory Pincus in the 1950s.

Margaret Sanger, the founder of Planned Parenthood, had asked Rock and Pincus to develop an oral contraceptive medication. To get FDA approval they would need to undertake large scale trials. However, this would not be possible on the mainland due to its restrictive laws on contraceptive research. So, they turned their eyes to Puerto Rico and a man called Clarence Gamble, heir to Procter & Gamble and friend of Sanger.

Following the US invasion of Puerto Rico in 1898, local farmers had their land taken away which meant that the island was struggling with poverty whilst also undergoing a population increase. After Franklin D. Roosevelt stopped funding birth control clinics in Puerto Rico as a result of pressure from the Catholic church, Gamble stepped in. With help from US Law 116, he started systemically sterilising Puerto Rican women in his clinics against their knowledge. He also set up clinics providing free sterilisations in factories, which then awarded jobs in favour of women who had undergone the procedure. This culminated in a third of Puerto Rican women being sterilised. What happened in these clinics was systemic eugenics and white supremacy, as Gamble and his colleagues said they were making room on the island for white people.

Rock and Pincus teamed up with Gamble as he already had the infrastructure to promote the pill. Women were told that the pill would stop them from getting pregnant but were not told they would be taking part in the first trial or that the side effects were not well understood. The pill given to these women was three times as strong as the one used today. Three women were recorded to have died but as no autopsies were undertaken it cannot be said if it was due to the early pill formulation.

These women had some benefit from the pill, but as it was taken without an understanding of it being a trial, it was unethical. In 2004, living participants reported bitterness at having been kept in the dark. Furthermore, the lasting cultural effect of Gamble's clinics can still be seen in Puerto Rico, where 39% of women in a marriage or union today have undergone sterilisation. Rates are still very high because the market price of the pill has not been accessible to many women on the island since it became commercially available. This is the case with any form of contraception or abortion care. To provide Puerto Rican women with the same reproductive rights as their continental counterparts there needs to be more effective subsidisation, education and trained healthcare professionals. Clinics should also be made more physically accessible to women living throughout the island. Mayra I. Díaz Torres is the director of one such clinic and is also fighting for trans-inclusive reproductive rights through the Aborto Libre campaign.

To clarify, what happened in Puerto Rico in the 1950s was not a one-off event. Just last year, news broke that unnecessary hysterectomies were carried out on women in an ICE detention centre. Also in 2020, two French doctors said they wanted COVID-19 vaccine trials to take place in Africa. They cited a higher participation rate as their explanation. This is despite the fact that in a low resource environment it is harder to obtain informed consent. Plus, these populations have higher participation rates because people know it might be their only chance at getting the vaccine. Is that really a choice?

There are two things that need to happen. More legislation needs to be put into place to protect vulnerable communities from historically eugenic practices, such as non-consensual sterilisation and drug testing. This includes detained people, migrants, people in existing and former colonies, disabled people, and those who do not speak the dominant language - essentially, anywhere where there is a power dynamic. Also, we need to work towards global equal access to pharmaceuticals, so people are not pressured into participating in trials out of desperation. Then, people worldwide will be empowered to make a real decision as to whether they want to participate in a trial or not.

Race-related stressors and their health impacts: How racism is making people sick

More than unease, race-related stressors could cause illness in the long run.

Written by Alice Ho Art by Lia Bote

Race has long been a topic of contention in mainstream media and academic discourse, and it remains so as the world sees a spike in reports of racial violence. However, in addition to immediate casualties and grievous injury, race-related stressors have also been harming racial minorities in more insidious ways.

Marginalised communities exhibit higher incidence, morbidity and mortality of diseases compared to non-marginalised communities. The idea that stress makes you sick is not new, but what's different here is that these health disparities are largely driven by environmental stressors rather than individual habits. Thus, there is a need to understand these stressors and how they cause negative health outcomes, so that they can be resolved.

It is helpful to classify race-related stressors into institutional and perceived racism. Institutional racism, also known as structural or systemic racism, refers to discrimination by major institutions and systems against racial minorities, such as education, employment, healthcare, and criminal justice. For example, the Social Metrics Commission reported that 46% of Black households in the UK are in poverty, compared to just under 19% of White households. Being disadvantaged in terms of nutrition, poverty, violence in the environment and psychosocial stress, it is no wonder that racial minorities have disproportionately poorer health outcomes. In the US, people of colour are more likely to live near areas of increased air pollution than White Americans. This puts them at higher risk of disease in virtually every organ in the body from the heart and lungs to the bones and skin. Hence, institutional racism limits access to healthy lifestyles and health services, contributing to racial health disparities. Conversely, perceived or interpersonal racism occurs at an ndividual level, taking the form of daily microaggressions, or one-off encounters with hate crime. They reduce self-esteem and create uncertainty about the future, resulting in greater psychosocial stress. These stressful experiences can begin early in life. In a 2019 study in Australia, 40% of year 5 to 9 students from non-Anglo or European backgrounds reported experiencing racial discrimination by their peers. In the UK, almost half the respondents to YMCA's 2020 Young and Black report felt that racism is the biggest roadblock to academic achievement. To assess the levels of perceived racism, hundreds of studies have used the Everyday Discrimination Scale, a questionnaire that tallies discriminatory encounters. Respondents who report a higher frequency of discrimination also tend to have poorer physical and mental health outcomes.

Besides institutionalised and perceived racism, race-related stressors can also be classified as acute or chronic, referring to instantaneous or short-term events and long-term challenges respectively.

How exactly do stressors affect health? One model indicates that dealing with racial discrimination leads to allostasis, where the body allocates energy towards physiologically adapting to short-term stress. In evolutionary terms, this is favoured because it delays somatic damage long enough to ensure survival and reproduction. However, it comes at a cost - frequently activating the stress response results in the deterioration of internal regulatory systems in the long run. This is known as 'allostatic load', which can manifest as chronic diseases, such as high blood pressure, diabetes and hypertension.

What is even more alarming is that these stressors, when experienced in childhood, can influence gene expression. The growing field of epigenetics has shed light on the dangers of race-related stressors during early development, where phenotypic plasticity is highest. If conditions such as maternal insulin resistance, hyperinsulinemia and diabetes are present during pregnancy, more insulin and glucose could be transported across the placenta, increasing the chance that the foetus experiences similar weight gain and metabolic dysregulation. Likewise, prenatal exposure to certain pollutants was linked to lower DNA methylation of a retrotransposon repetitive element in the human genome. Importantly, these poor health outcomes are due to environmental stressors, not innate genetic differences women of African descent born abroad were 25% less likely to have an infant with low birth weight, compared to those born in the US. This difference was absent between White women.

In light of COVID-19, the existing health disparities have become even more obvious. Firstly, research shows that BAME communities in the UK are more susceptible to conditions such as diabetes, obesity, asthma, and depression, which in turn puts them at higher risk of severe COVID-19 disease. Secondly, due to allostatic load, individuals have a poorer stress response, which directly leaves them more susceptible to COVID-19. This could in part explain why the mortality risk was twice as high in Black communities.

While the problem of race-related health stressors is a complex one, there are ongoing efforts to devise and implement solutions. At UCL's own Centric Lab, research projects are underway, aiming to "help rehabilitate people through better urban policy and public health strategies that support our health". In addition to providing educational resources, the Centric Lab designs and executes initiatives such as Know Your Health, a website and guide document created in collaboration with PLP Labs and design studio COMUZI. Here is how it works: individuals are encouraged to enter their address, and receive feedback about the potential environmental stressors they face. Next, they are offered a chance to advocate for change in their neighbourhood and those nearby. The project emphasises raising awareness among the local community about their own health, and allowing them to stand up for it.

There is an urgent need for further research on how complex biological mechanisms enable race-related stressors to impact health. In order to promote better public health, underlying stressors and their mechanisms must be understood and accounted for by professionals across all disciplines - medical staff, policy makers - and affected communities themselves. Most importantly, the best solutions should be made by incorporating voices from the community, instead of taking a top-down approach and relying solely on what officials believe works best.

Addressing the UK's Dementia Dilemma What's Happening and What's to Come?

Dementia is a major issue in the UK – what has the government done to address this dilemma and what hope is there for the future?

Written by Similoluwa Ayeniyegbe Art by Lola Artiles

Major medical advancements have resulted in longer life expectancies. Although medical advancements are worth celebrating, with longer life expectancies comes an ageing population, so dementia has become a pressing issue in the UK. Many people reduce their working hours in order to care for their loved ones and others leave work altogether, resulting in significant economic losses. Currently there is no cure for dementia, which is partly related to the brain's complexity and the wide range of symptoms, both of which make clinical trials challenging to conduct. But what has the UK Government done to address this dilemma?

In 2011, a Dementia Commissioning Pack was launched, which contains resources for health and social care commissioners to improve the quality of dementia services for patients and their carers. It was developed after consulting people living with dementia and their carers, advocacy groups and health and social care commissioners. The pack addresses dementia services from diagnosis until end-of-life care. Besides dementia care, however, the UK Government has launched initiatives aiming to advance dementia research.

The Dementia Discovery Fund was established in 2015 - a £250 million specialist venture capital fund with the aim of supporting future dementia treatments. The fund was established with the UK Government's Department of Health and Social Care in collaboration with companies such as GlaxoSmithKline and the charity Alzheimer's Research UK. This was the first venture capital fund solely focused on dementia research.

In 2019, the Dementia Discovery Fund and Alzheimer's Research UK established a biotech company called AstronauTx. AstronauTx focuses on developing medicines which target astrocytes to treat neurodegenerative diseases. Astrocytes are a type of glial cell found in the central nervous system and have been implicated in Alzheimer's disease (the most common form of dementia). The exact functions of astrocytes in Alzheimer's disease are not fully understood, meaning that the research conducted by AstronauTx could be invaluable. What else could be done to improve the lives of people with dementia?

Evidence-based medicine is the explicit and reasonable use of modern evidence to inform decision-making about the care of individual patients. Adequate dementia care for an individual patient can be achieved when physicians combine their knowledge of best available evidence for dementia diagnosis with their clinical skills. Specifically, memory tests are often a key test required to diagnose dementia, however research suggests that this may not be the best way to identify the syndrome.

In the UK, positron emission tomography (PET) scans are occasionally used, but increased use could lead to more definitive dementia diagnoses. In Alzheimer's disease, amyloid beta plaques accumulate in the brain. Amyloid PET imaging can help to map the spatial distribution of this brain pathology. Besides being helpful for diagnosis, determining the presence of amyloid beta pathology can also be used to monitor disease progression and for prevention studies. In clinical trials, PET scans have improved diagnostic certainty, so their widespread use in clinics could be invaluable for diagnosing and monitoring dementia. PET imaging is just one of various techniques that could increase our understanding of the syndrome.

Whether our understanding of dementia improves via PET scans or other research angles, a better understanding is crucial to improve treatment. Could this take us one step closer to resolving the UK's dementia dilemma?

The Responsibility of Scientists in the Anthropocene

Scientists must engage in politics to overcome the challenges of the Anthropocene

Written by Adhiyan Jeevathol Art by Lia Bote

At the beginning of this year, an event of considerable human importance occurred. The doomsday clock, a metaphor for global catastrophe, was moved by the Bulletin of the Atomic Scientists to 100 seconds until midnight. Describing it as "The most dangerous situation humanity has ever faced", Edmund G. Brown and Robert Rosner from the Bulletin cite the prospects of nuclear war and environmental catastrophe as the primary reason for our dire state of affairs. Both these problems are, in part, a result of our scientific knowledge. With the increase in scientific power, both the good and evil in human nature have been magnified culminating in the nuclear age, where the threat of nuclear war looms large, and a new geological epoch, called the Anthropocene, where human actions are altering the Earth's geology and ecosystems.

Considering this, it is natural to ask what is the responsibility of scientists in the Anthropocene.

Writing in 1968, the public intellectual and author Paul Goodman argued that scientists should "engage in political activity to try and undo the damage that they have cooperated in producing". Scientists don't just have this responsibility because of their complicity in creating our current condition. According to the linguist and philosopher, Noam Chomsky, such a duty also arises from the privileges they have over the average person as he explains in his essay Responsibility of Intellectuals: intellectuals "have the power that comes from political liberty, from access to information and freedom of expression. For a privileged minority, Western democracy provides the leisure, the facilities, and the training to seek the truth". Thus, for Chomsky "It is the responsibility of intellectuals to speak the truth and expose lies."

Scientists have, by and large, spoken the truth by warning the public of the issues we face, but the impact of this has been limited. Even today, climate change and nuclear war scarcely receive the attention they deserve. Though his tweets received widespread coverage, Trump's intention to withdraw the US from the major nuclear arms treaties was barely an issue during the Presidential election. Similar attitudes are prevalent elsewhere. Speaking about Israel's response to predictions that the region will become uninhabitable due to climate change, the leading Israeli environmental activist Professor Alon Tal observes: "The Jewish state has looked humanity's ultimate challenge in the eyes and said: 'Forget it.'"

This is because the truth has often been drowned out by the lies and distortions that emanate from politics and even from the intellectuals themselves who, according to Chomsky, present a certain conception of reality to the general population. This in turn creates the "ideological justification for social practice". In relation to climate change and nuclear war, this 'social practice' has been apathy. For example, in his 2018 Nobel Prize lecture, the climate change economist William Nordhaus presented the 'optimal' path for addressing climate change. In this scenario, the global average temperature would increase by 2x as of 2050 (despite the IPCC report advocating a maximum of 1.5x) and 4x by 2150. Shockingly, Nordhaus claimed that we should accept the risks of a rise in 4 degrees. Science journalist Mark Lynas explains the consequence of this apathy: "Whole areas, and indeed whole island nations, will be submerged. In Europe, new deserts will be spreading in Italy, Spain, Greece, and Turkey: the Sahara will have effectively leapt the Straits of Gibraltar."

Steven Pinker, the widely acclaimed author and intellectual, is another case in point. For Pinker, human history is becoming increasingly rational and so, there's little reason for panic. But his premise is faulty. As an example, he explains how the Cuban nuclear missile crisis of 1962 was only avoided by Kennedy and Khrushchev's "intuitive grasp of game theory". One wonders, however, where this rationality went in the creation of the missile crisis and where it's gone as our eminent statesmen have continued to escalate the threat of nuclear war.

By downplaying the scale and urgency of the issues we face, these are the kind of intellectuals that encourage humans to say 'forget it' while looking 'humanity's ultimate challenge in the eyes'. Scientists, who retain some authority in the eyes of the public, are in a good position to confront this by engaging in political work that will reverse this apathy.

However, political engagement should not only be considered by official scientists. Many of us at UCL also have the 'political liberty', 'access to information', 'freedom of expression' and 'training' to 'speak the truth and expose lies' and so we too must confront similar questions of responsibility.

Such questions will become ever more important as scientific knowledge progresses; with it so will our power to destroy and create. Avoiding the former will need a corresponding increase in wisdom which will inevitably require scientists to engage in politics. The pandemic has given us an insight into the consequences of apathy but, as the Bulletin of the Atomic Scientists explain, the disease will eventually recede. However, with the looming threat of nuclear war and climate change, next time the doomsday clock may actually strike midnight. Much will depend on how scientists meet their responsibility in the Anthropocene.

THE LEGAL DRUG BOSSES

Who controls how much we pay for our drugs and why it matters.

Written by Tara Spasojevic Art by Priyanka Peres

The most expensive drug in the world is Zolgensma. It costs £1.79 million per dose. It is a gene therapy for infants under 2 years old with spinal muscular atrophy, which is a rare and often fatal disease. As many as 80 babies and children could benefit from this per year in the UK. Imagine if you or a loved one needed Zolgensma. Luckily, UK citizens benefit from the National Health Service (NHS), which spends about £18 billion a year on drugs.

A drug can be simply defined as a chemical that when administered to the body produces a change or biological effect in the organism. A medication is a drug used to prevent or cure disease. Medicines or pharmaceuticals are produced by pharmaceutical companies which will then sell them to the rest of the world.

Drug prices are constantly changing based on multiple factors. Newly released drugs are protected by patents, thus, other companies are unable to manufacture the same therapeutic agents. However, after 20 years, the patents expire. At this point the drug can be snapped up and produced by any other pharmaceutical company.

Such drugs are known as generics and they work in the exact same way as the brand-name drug. Manufacturing generics eliminates the need for lengthy and expensive preclinical and clinical trials, including animal testing. This dramatic reduction in research costs means that, crucially, the generic drugs are sold at much cheaper prices – around 85% less than the brand name. Nurofen costs almost 5 times more than Boots' own brand ibuprofen which retails at £0.03 per 200mg tablet – both have the same effect and the same active ingredient.

Generic drugs have saved the NHS around £320 million a year. Adalinumab (Humira®), a biological drug, administered for the treatment of Crohn's disease and rheumatoid arthritis, used to be the most expensive drug used in NHS hospitals. Nonetheless, in 2018, Humira came off patent allowing the production of biosimilars (this is the 'generic' form of biological drugs which are somewhat more complicated). This is expected to save the NHS at least £150 million a year.

The NHS is the major buyer of pharmaceutical products in the UK. There is a set price for NHS-prescribed drugs that was introduced in 1949, and in recent times all prescriptions have been made free

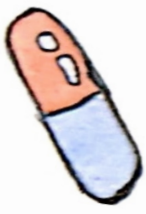
of charge in Scotland, Wales and Northern Ireland. Whereas in England, the prescription charge rose by 20p in April this year to £9.35 per prescription item. There is an exemption from the prescription charge, which, in England, encompasses 40% of the population – including all over 60s and full-time students below 18 years old (sadly not university students). As a result, over 90% of prescription medications are actually being dispensed free of charge.

When a pharmaceutical company develops a new drug for the UK market, they first must face the dragon guarding the gold – better known as the Medicines and Healthcare products Regulatory Agency (MHRA). The MHRA regulates the pharmaceutical market based on the significance and benefit of the new drug compared with the existing options with respect to the price of the new drug. In the US, the story is different. The Food and Drug Administration (FDA) regulates the safety and effectiveness of drugs but has no authority on cost-benefit regulation. This means that every drug approved by the FDA goes on the US market at the price the manufacturer sets.

Although it seems handy to have access to a wide range of drugs, the US has the highest drug prices in the world. Hence, many people simply can't afford prescribed medication. Humira® costs twice as much in the US as it does in the UK. What's more, studies have found that drug prices are higher in pharmacies in less affluent postal codes, further exacerbating disparities in drug access.

Insulin is ten times more expensive in America compared to the rest of the world and its cost has risen by over 1000% since 1999. Patients with type I diabetes need insulin to survive and will pay large amounts for it, which is easily exploited in a system with no regulations. Unfortunately, not all are able to do so. In some cases, patients have attempted to ration their insulin supplies to make their 'money go further', which has resulted in their untimely deaths.

Overall this sounds pretty horrific, although there is a catch. High drug prices in the US have meant more money being pumped into drug research. The more research, the more new or improved treatments are discovered, which benefits the rest of the world. The US contributes to 43.7% of novel drug discovery.



Drug demand is rising, but so are prices. What's more, a post-Brexit UK-US trade deal could add additional costs of £519 million per week – that's £27 billion on top of what the NHS is already paying per year, in the worst case scenario. Does more money spent on drugs mean lighter pockets for individuals and governments alike, or does it mean more drug discovery? Hopefully the latter will hold true.

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