TECHNOLOGY NETWORKS

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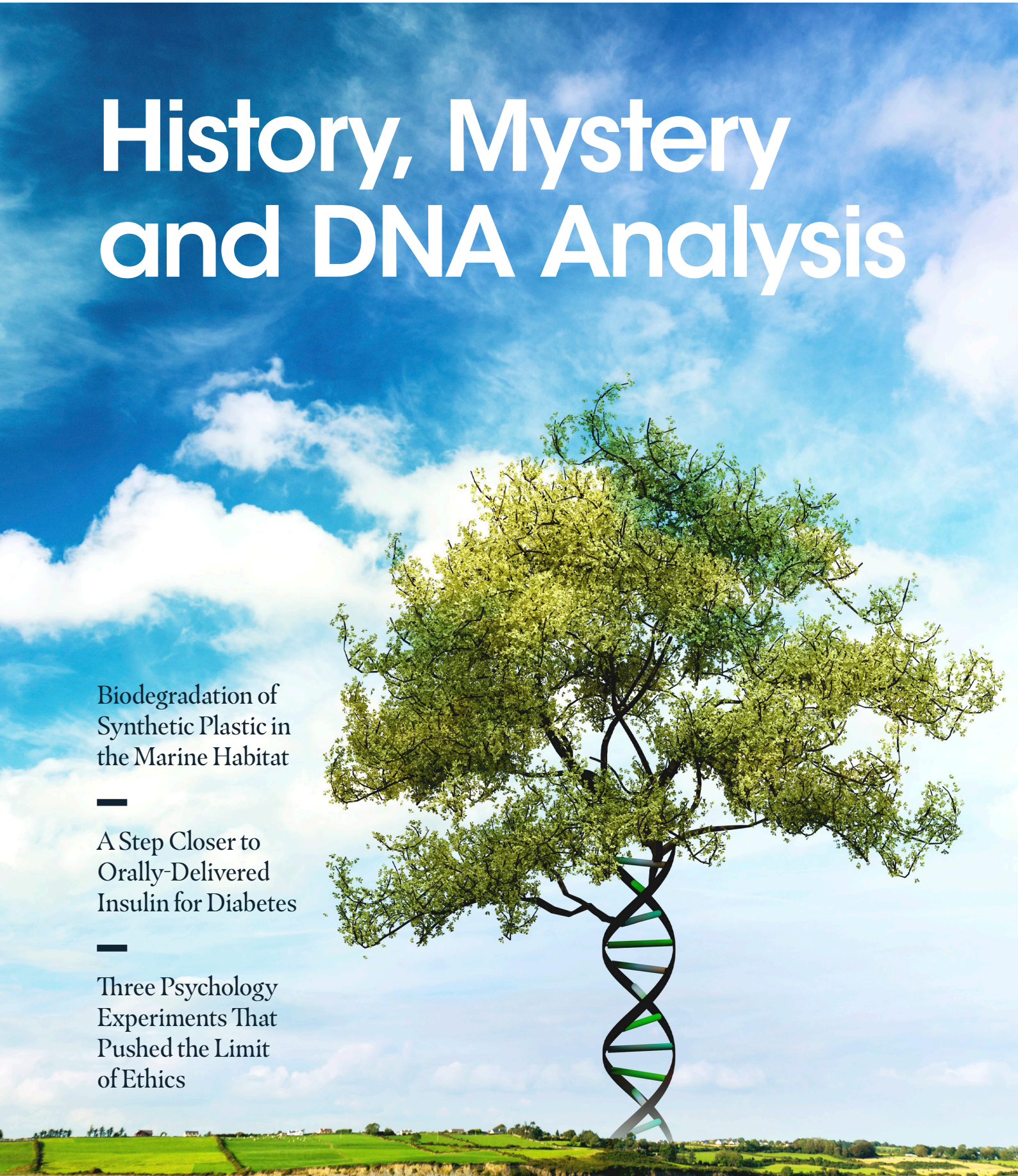
History, Mystery and DNA Analysis



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Molly Campbell

EDITORS' NOTE

Welcome to the second issue of *The Scientific Observer*, a new editorial venture brought to you by *Technology Networks*. Each month, we explore key themes and topical issues by combining a selection of our favourite scientific stories from the *Technology Networks* communities with new and exclusive content.

This month's issue places emphasis on the fact that scientific research is *always* a work in progress. Join us as we explore pertinent issues of the past, present and future of science, including the impact of synthetic plastic in the marine environment, psychology experiments that pushed the limits of ethics and the advances in tissue engineering that are accelerating the field of drug discovery.

If – like us – you are a fan of historical mysteries, make sure you check out this month's feature article. Post-mortem analysis of the 1845 Franklin Expedition continues over 176 years after HMS *Erebus* and HMS *Terror* departed from British shores. Can modern DNA analysis finally provide academics, scholars and descendants of the men who perished with some answers as to what happened on the ill-fated voyage?

There are glimpses of "normality" returning to certain areas of the world as COVID-19 vaccine distribution and administration continues, but logistical issues remain. Looking to the future, Priyom Bose and Michael Kinch discuss scale-up and patent-related challenges that must be addressed as we work to immunize the global population.

If you have an idea for a story, or you would like to contribute to *The Science Observer*, please feel free to email us at any time – editors@technologynetworks.com.

MOLLY CAMPBELL

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Biodegradation of Synthetic Plastic in the Marine Habitat

YI ZHANG

The marine environment is quite different from the land ecosystem in terms of temperature, oxygen concentration and light intensity, among other factors. Biodegradation of plastic waste on land can proceed over decades. The question then is what happens to the plastics in the marine environment? The estimated 5.25 trillion plastic pieces floating on the ocean surface[1] have been identified as a serious global health issue. The accumulating data on marine plastics give us a better appreciation of the challenges and opportunities with biodegradation of plastics by marine microbes and their enzymes and its potential to be employed in marine plastics treatment.

THE "MISSING" PUZZLE OF PLASTIC LITTER IN THE OCEAN

Approximately 1.5 to 4.1% of the plastics produced globally enter the oceans both intentionally and unintentionally; thus, a total of about 117 to 320 million tons of plastics are present in the ocean.[2] This amount of plastic litter would be sufficient to wrap up a medium-sized country in Europe.

The plastic wastes on land are typically collected and treated in various ways, including dumping in landfills, incineration, granulation and pyrolysis. However, plastics finding their way into the oceans have an entirely different fate, with humans practically unable to manipulate marine plastics on a large scale currently.

Although there is a lack of technologies to detect, monitor and quantify plastics floating on ocean surfaces or settling on the ocean floor, scientists have enough evidence to suggest that a large bulk of the plastics in oceans are "missing".[3] So, where do or did they disappear to?

As attested to by the hundreds of distressing pictures depicting an unusual intermingling of marine animals and synthetic plastics, some of the plastics in the oceans are ingested by or become intertwined with marine species. The other explanation for this puzzle is degradation.

BIODEGRADATION OF MARINE PLASTICS

Plastics are degraded in the ocean through three pathways:

- Mechanical degradation (break-down of large plastic pieces into smaller plastic fragments by mechanical action)
- Photodegradation (via free radical chain reactions initiated by solar UV radiation)
- Biological degradation or biodegradation (by microorganisms in the marine habitat)

Data on the degradation extent and the degradation products from photooxidation and biodegradation of plastics in the oceans are relatively limited.

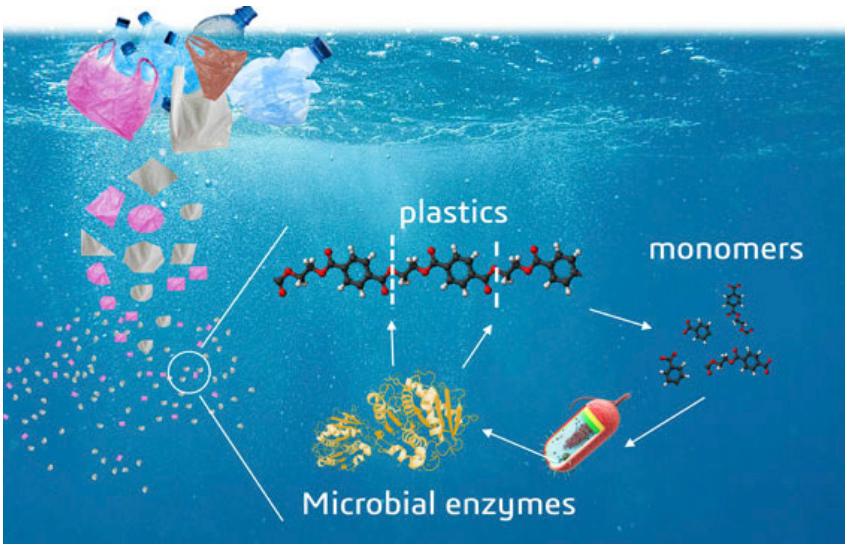
Model studies on plastic photodegradation suggest that it could take several years to degrade into microplastics or nanoplastics and it could take hundreds of years for plastics to disappear completely (for example, into hydrocarbon gases).

Biodegradation of plastics relies on the marine microbes. Since the first introduction of plastics into oceans in the 1950s, some marine microorganisms, namely bacteria and fungi, have shown a capacity to adapt and evolve to utilize plastics as a source of carbon and/or chemical energy. The microbial communities colonizing marine plastic surfaces, which are also referred to as plastispheres are unique and different to those from the surroundings. Microbial populations on plastispheres favor plastic degradation[4] and thus, plastispheres have been a focal point to discover microbes able to degrade plastics in the marine environment.

Microbial degradation of plastics requires enzymes capable of breaking down plastic materials into oligomers, dimers and monomers, as presented in Figure 1, below.

One such famous plastic-degrading enzyme, polyethylene terephthalate (PET) enzyme (PETase), was first discovered from *Ideonella sakaiensis* collected in a PET bottle recycling sludge in Japan in 2016.[5] Recent finding suggested that the increasingly available plastics in the ocean have driven a rapid evolution of oceanic PETases globally.[6] This enzyme catalyzes the cleavage of PET into monomeric mono-2-hydroxyethyl terephthalate (MHET) which can be further degraded into non-hazardous monomers by another enzyme, MHETase. PETase can shorten the degradation of PET from decades to days. Other enzymes found with capacity to degrade plastics include amidases, oxygenases, laccases, peroxidases, lipases, esterases, cutinases and serine hydrolases. Therefore, plastic monomers could also provide a carbon source for marine microbial communities, traversing the cell membrane and subsequently being oxidized during microbial metabolism, resulting in the release of CO_2, N_2, CH_4, and H_2O.

Although knowledge about plastic biodegradation in the ocean in terms of the rate, process and mechanisms is still scarce, the information known and lessons learnt from recent studies provides opportunities to explore and develop microbial plastic degradation as a natural bioremediation strategy to remove plastics from the marine environment. Due to the unique environment in the ocean, non-conventional bioremediation techniques need to be designed to allow sustainability development. A synthetic biology approach, encompassing gene editing, genetic engineering and other omics techniques, alongside the discovery of naturally capable microbes may be appropriate to develop a symbiotic community of microbes able to degrade plastics efficiently in the marine environment.[7] Moreover, the oxidized gaseous products from a microbial population could be recycled and reused. One estimate reported that approximately 23,600 metric tons of dissolved organic carbon generated annually from marine plastics can stimulate the activity of heterotrophic microbes in seawater, which may change the ocean ecosystem.[8] In this regard, bioremediation of marine plastics based on microbe- and enzyme-driven biodegradation may have potential. ●



Biodegradation of marine plastics by marine microbes and their enzymes.

Credit: Yi Zhang, PhD

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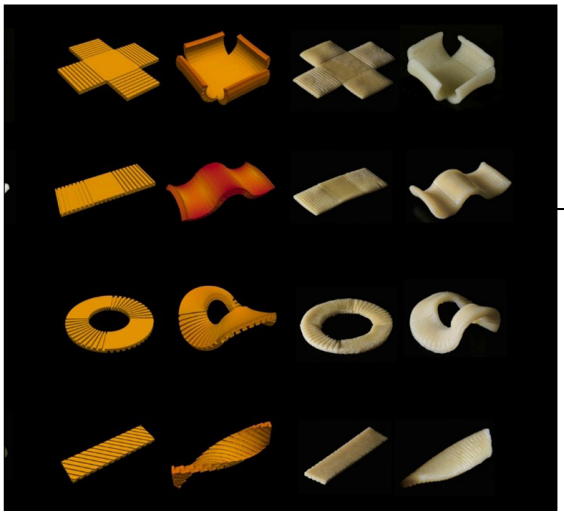
From the Newsroom

BEHAVIORAL EFFECTS OF ALCOHOL MAY BE CAUSED BY BREAKDOWN PRODUCTS PRODUCED IN THE BRAIN

LAURA ELIZABETH LANSDOWNE

Researchers have demonstrated that alcohol metabolism can occur in the mouse brain, due to the presence of the enzyme aldehyde dehydrogenase 2 (ALDH2). They also found that expression of ALDH2 in the mouse cerebellum mediates behavioral effects related to alcohol intoxication.

JOURNAL: *Nature Metabolism*

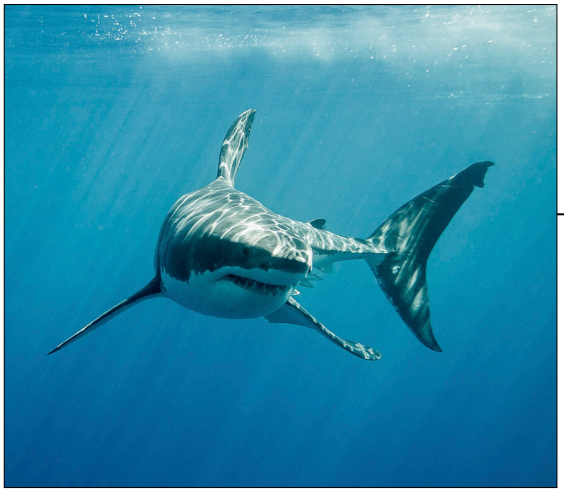


FLAT-PACKED PASTA – A MORE SUSTAINABLE WAY TO ENJOY YOUR PENNE?

MOLLY CAMPBELL

Researchers from the Morphing Matter Lab at Carnegie Mellon University propose a new approach to enjoying your penne: flat-packed pasta that morphs into the shape of "traditional pasta" when it is cooked. Inspired by flat-packed furniture, the scientists hypothesize that this approach could offer a space-saving solution for transporting pasta, which might reduce the carbon footprint of the process.

JOURNAL: *Science Advances*



LIKE SEA TURTLES, SHARKS USE THE EARTH'S MAGNETIC FIELDS TO NAVIGATE

RUAIRI MACKENZIE

When they aren't clogging up airtime on the Discovery channel or being unfairly maligned as threats to human life (hippos, who weigh 3,000 lbs and can sprint, are much, much deadlier), sharks spend their time swimming in migratory patterns. A new study suggests that sharks, much like sea turtles, sense the Earth's magnetic field to navigate around the ocean.

JOURNAL: *Current Biology*

Credit: Morphing Matter Lab, Carnegie Mellon University.

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Grieving in Isolation

ANONYMOUS

The "stay-at-home scientist". It conjures images of some 19th century alchemist working in the loft of some eccentric benefactor, surrounded by bizarre and exotic equipment. If only this were the case. I am currently surrounded by my desktop, my laptop and a clothes airer full of yesterday's baby grows. I work in the back bedroom, also known as the "dumping ground". The room where our possessions go only to gather dust and slowly be forgotten about. I realize bemoaning the state of my spare bedroom and its suitability as a home office is a major first-world problem. Nevertheless...

Some jobs really lend themselves to working from home. Scientists that work on large datasets are often able to work from home, searching for trends and re-slicing data. Molecular biology is difficult to do from home. Prior to COVID-19 I would have the odd day working from home if I had a lot of writing to do, or a particularly intense set of analyses to complete. This was usually met with a raised eyebrow from bosses who clearly suspected that not much work would get done.

Then the world changed. We strongly suspected that there would be an enforced period whereby we would not be allowed access to the laboratory. There was a mad flurry of colleagues doing experiments to generate large amounts of data that we could then pour through at our leisure from home.

Two days prior to the first national lockdown, I was in a pharmacy fighting through crowds of people buying cold and flu medicine to buy a pregnancy test. We found out my wife was pregnant, which was obviously fantastic news, but was met with some trepidation. My then two-year-old son's nursery shut, and my wife and I were faced with each of us working from home and sharing care responsibilities for our little boy.

Then my 32-year-old brother died of COVID-19. My seemingly fit and healthy sibling, who had no known underlying health conditions, was taken in his prime by the pandemic. This felt and still feels like a medieval way to die. So, there we were; grieving in isolation, working remotely and looking after our boy who had no idea why he couldn't see his friends.

Like most scientists, early on in lockdown I had made grand plans to write papers and grant applications. This was tricky; as part of the writing process I would spot holes in my work that could be easily solved by performing small experiments. Of course, no matter how small or simple the experiment, it was impossible to do from home. I did manage to submit a manuscript and focus a few other plans. Once this was done, I was twiddling my thumbs a little bit.

I missed my colleagues. Little chats here and there really break-up the day. I found it hard to focus. We faced an enforced absence from the lab for around three months. We have been allowed access to the lab for nine months or so now, albeit under heavily prescribed conditions. Don't get me wrong, I completely agree with the stipulations and am somewhat reassured by their presence. However, progress is slow compared to how things were before. We must book lab space to ensure we work in a specified area, must not come within two meters of someone else and have to wear a mask in and around university buildings. The problem is that we often must wait to find a slot to book a particular area. Also, it is tricky to know which areas of the lab we will need.

Personally, I find I can plan Monday to Wednesday morning. My work thereafter usually depends on the results I have obtained earlier in the week. Our bosses' expectations remain at pre-pandemic levels. They have been working from home and have not returned to university buildings. Therefore, they have little understanding of the current conditions we are working under. Booking areas and trying to work around each other is inherently inefficient. Everyone is trying their best, but there are obviously last-minute ideas that must be shelved until one can book the appropriate area.

My wife has been on maternity leave since December, and it has been great – though terribly distracting – to be around the house more. It has been hard to stay in my "office" if I can hear our daughter crying and think my wife could do with some support. Though I do count myself as very lucky.

It is astounding how much I took for granted. I miss being able to work in the lab around my colleagues all day, without booking areas and wearing masks. I am looking forward to being able to return to the "old normal". ●

TECHNOLOGY NETWORKS

Don't Keep Your Opinions to Yourself

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Three Psychology Experiments That Pushed the Limit of Ethics

RUAIRI MACKENZIE

Last month, a team of volunteers emerged from 40 days of isolation in the Lombrives cave in southwest France. This ordeal was part of a scientific study called the Deep Time experiment. The volunteers were tasked with going without sunlight, phones or clocks for the duration of the experiment. The study aimed to understand how the human brain would be affected as it lost its grasp on time and space. Putting human subjects, even volunteers, through this might seem ethically dubious, but pales in comparison to the questions raised by these three studies.

THE ULTIMATE ISOLATION: HEBB'S "PATHOLOGICAL BOREDOM"

Until COVID-19 lockdown gave everyone an unwanted taster session, extreme isolation was an experience traditionally reserved for long-term prisoners and extremely committed polar scientists. But in 1951, Donald Hebb, a neuroscientist whose discoveries about the brain redefined what we know about learning, undertook a series of tests that would push volunteers into a near-total solitude.

Hebb and his team designed a setup that would isolate test subjects not just from other people, but from virtually all perceptual stimulation. The subjects, for the (relatively generous at the time) sum of $20 a day, were tasked with lying in bed in a small, lit cubicle for 24 hours a day. Breaks were given at mealtimes (eaten sitting on the edge of the bed) and for toilet breaks. The volunteers wore visors that allowed in light but blocked any detailed vision, and touch-restricting cotton gloves. A continuous hum of air conditioning masked any small sounds that might have broken their sensory cocoon.

Hebb and his team wanted to see how this environment, one that wasn't entirely devoid of sensory information, but that was incredibly monotonous and boring, would affect the volunteers. Initially, the participants, who were all university students, thought about their results, or the papers they had due. But after a while, their minds instead drifted onto memories from their childhood. Eventually, most of the participants reported that they became unable to think about anything for any length of time. These details were reported by Hebb's collaborator Woodburn Heron in an article published in *Scientific American*. The subjects also showed impaired mental performance, registering lower results on tests of mental arithmetic and word association.

Most strikingly of all, the subjects reported that, despite their complete absence of sensory stimulation, they experienced an array of hallucinations, including one participant who saw endless images of babies. These hallucinations, which Heron compared to the effects of the hallucinogenic drug mescaline, grew in complexity over time – one participant eventually reported "a procession of squirrels with sacks over their shoulders marching 'purposefully' across the visual field."

The hallucinations were accompanied by sounds and even sensations across the volunteers' bodies. Summing up these weird and distressing effects, Heron concluded that "a changing sensory environment seems essential for human beings."

HOW MALLEABLE IS OUR WILLPOWER?

Perhaps the most infamous psychology trial, the Milgram experiments were conducted by Yale University's Stanley Milgram in 1961. The experimental setup involved an experimenter, a volunteer dubbed the "teacher" and an actor, who pretended to be another volunteer – the "learner". The teacher was told that they were participating in a test of learning and memory that would investigate how well punishment encouraged ability. They were placed in front of a series of buttons representing different levels of electric shock that they were told would be delivered to their fellow "volunteer", who was strapped into what appeared to be an electric chair in an adjacent room. The teacher was told that they were to conduct a word test with the restrained learner and were to shock them if they made any mistakes. The buttons, which included warning labels for the intensity of the "shock" they gave, were meant to deliver up to a dangerous 450 volts of stimulation.

Most strikingly of all, the subjects reported that, despite their complete absence of sensory stimulation, they experienced an array of hallucinations, including one participant who saw endless images of babies.

In 2008, the BBC attempted to re-enact Hebb's experiments.

Credit: BBC Horizon.

The buttons, of course, did nothing, but the actor was trained to respond with increasingly agonized reactions to their "shocks". The teacher, encouraged by the lab coat-wearing experimenter was, in reality, being tested for their level of obedience – an experiment that aimed to understand whether individuals who have carried out horrendous crimes, such as Holocaust architect Adolf Eichmann, could really have just been "following orders".

The teacher could not see the learner, but as the "shocks" increased, pre-recorded shrieks of agony were played over a loudspeaker, and the learner eventually started banging on the separating wall in protests. At the highest voltages, the "shocked" learner fell silent.

Milgram's findings were remarkable. The teachers moved through the voltages at the behest of the experimenter, who gave increasingly strident instruction – eventually telling them, "You have no other choice; you *must* go on."

The experiment only ended if the teacher refused this highest level of instruction, or if they delivered the highest voltage three times in a row. To the research team's amazement, 26 of 40 participants proceeded to the highest voltage. Whilst the participants often reacted with horror to their instruction, with some breaking out in laughing fits and even seizures, all administered at least 300 volts

to their learners. Milgram reflected on these controversial experiments years later in his book *Obedience to Authority: An Experimental View*, where he summarized that his trials showed "the capacity for man to abandon his humanity, indeed, the inevitability that he does so, as he merges his unique personality into larger institutional structures." More recent analysis has thrown Milgram's subjectivity into doubt, as summarized by psychologist Gina Perry.

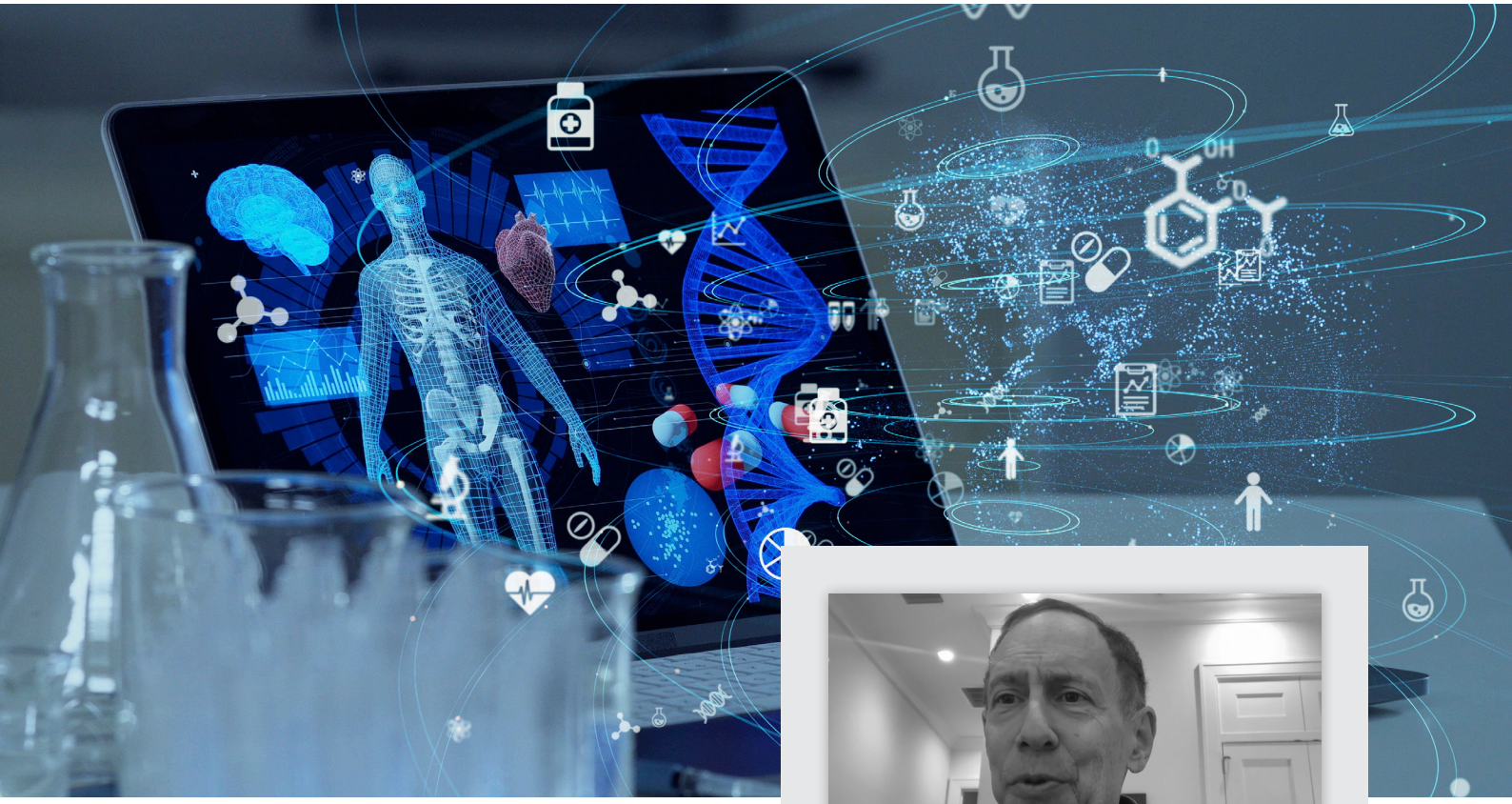
THE FACEBOOK STUDY: HOW CONTAGIOUS ARE EMOTIONS?

A much more recent, but equally controversial study, looked at the how human emotions could become "contagious" to others with relative ease. This study didn't rope in unwitting university students, but instead involuntarily recruited nearly 700,000 Facebook users.

The study, which was published in the *Proceedings of the National Academy of Sciences,* had a simple aim. The authors, members of Facebook's Core Data Science Team, wanted to test whether seeing positive emotions online would make users happy, or whether it would make them sad as a kind of spiteful reaction, as had been previously theorized. The team were given the power to alter the emotional content of their subjects' Facebook feeds over a week in 2012. They found that when feeds were biased in favor of negative emotions, users started posting more negative content themselves. When happier emotions were shown, the opposite happened. No fake content was used, but rather the team simply changed the feed's algorithm so that certain types of content were filtered out.

Whilst these findings were interesting, the ethically dubious way in which the study was conducted makes for uncomfortable reading.

This study started huge controversy when it was ascertained that the only consent Facebook sought was signing up for the platform. Facebook's Data Use Policy, the company said, gave them all the permission they needed to play around with users' feeds. Whilst these findings were interesting, the ethically dubious way in which the study was conducted makes for uncomfortable reading. The ethical quandaries involved, and the reasons why the study was able to bypass certain regulations, were summed up by bioethicist Michelle N. Meyer in an article for *WIRED*. ●



Materials for Drug Discovery

WITH PROFESSOR ROBERT LANGER

LUCY LAWRENCE

We are making it easier than ever to access complex areas of science and to learn something new. *Teach Me in 10* challenges scientists to present and summarize their research, or a scientific concept, in less than ten minutes. Our feature episode for the May issue of *The Scientific Observer* is "Materials for Drug Discovery" with Professor Robert Langer.

In the 1960s, materials that were not designed for the human body were often used for medical purposes. Breast implants were originally made from mattress stuffing, and the materials from ladies' girdles were used in the first artificial hearts, for example. Medicine has come a long way since then, and our guest, the renowned Professor Robert Langer, has played a large part in this.

Langer is one of few Institute Professors at the Massachusetts Institute of Technology, has written more than 1,500 articles and has over 1,400 issued and pending patents worldwide. His patents have been licensed or sublicensed to over 400 pharmaceutical, chemical, biotechnology and medical device companies. He is also the most cited engineer of all time.

Langer has played a critical part in developing new families of plastics that lead to pioneering treatments for brain cancers, drug-eluting stents, transdermal patches. In this *Teach Me in 10,* he tells us how these are adopted in modern drug delivery.

Langer also discusses tissue engineering and how he has used materials to make new skin to treat burns victims, created new blood vessels to treat diabetes and repair spinal cords and has even used tissue engineering to encourage hair cells in the ear to proliferate, helping people who have lost their hearing, to hear once again. ●

A Step Closer to Orally-Delivered Insulin for Diabetes

LAURA ELIZABETH LANSDOWNE

Diabetes is a metabolic disease that results in an increase in blood sugar also known as hyperglycemia. The prevalence of this disease continues to increase, with the World Health Organization (WHO) stating a rise from 108 million affected in 1980 to 422 million in 2014, highlighting the importance and significance of treatment. Combined with changes in lifestyle, insulin therapy continues to play a vital role in controlling and regulating blood glucose levels, with injection being the primary means of delivering the hormone. However, this administration route is much more invasive compared with oral drug delivery, meaning those diabetes patients with a fear of needles and/or self-injection, may be unwilling to begin insulin therapy.

Technology Networks recently had the pleasure of speaking with two authors of a *Chemical Science* paper, Farah Benyettou and Ali Trabolsi to learn more about the advantages of delivering insulin orally. Benyettou and Trabolsi elaborate on the intricacies of the imine-linked-covalent organic framework (nCOF) nanoparticles they are developing and discuss how this approach can help to overcome key barriers associated with the oral administration of the drug.

Q: What are some of the challenges associated with delivering insulin subcutaneously via injection?

A: Coupled with lifestyle changes, insulin therapy remains a key element in controlling and regulating blood glucose levels of diabetic patients. The primary mechanism to do so is insulin injection. However, studies have shown delays in onset of insulin therapy in a large proportion of people with uncontrolled diabetes, and in those who do eventually undertake treatment; there is a delay of more than two years from first administration.

Reasons why people are unwilling to start insulin therapy can include a fear of needles and self-injection, as well as pain and anxiety. Insulin pens alleviate some of these conditions, as well as overcome dosage issues that exist with vials and syringes; however, this method is not error-free.

Q: What are the key advantages to oral delivery of drugs, more specifically, can you elaborate on the oral bioavailability of insulin?

A: Orally-delivered insulin is capable of reaching the systemic circulation after passing through the liver, similar to physiological insulin secretion, while subcutaneously injected insulin may result in peripheral hyperinsulinemia and associated complications.

A shift towards oral delivery of insulin has the potential to improve the uptake of insulin therapy and revolutionize diabetes care, since it is a non-invasive therapeutic approach that does not cause the side effects caused by frequent subcutaneous injection.

However, oral drug delivery faces numerous challenges including dissolution, bioavailability, solubility and its stability in the gastrointestinal (GI) tract. The oral bioavailability of insulin is severely hampered by its inherent instability in the GI tract and its low permeability across biological

membranes in the intestine (less than 1%). Despite clinical trials of several oral insulin formulations, sufficient commercial development has not been yet achieved.

By using prepared layers of nanosheets with insulin loaded in between each layer, it is possible to protect it. Using this technique, researchers have now developed gastro-resistant imine-linked-covalent organic framework nanoparticles (nCOFs) that exhibit insulin protection in the stomach as well in diabetic test subjects, whose sugar levels completely returned to normal within two hours after swallowing the nanoparticles.

Q: Why has sufficient commercial development of an oral insulin formulation not yet been achieved?

A: To be considered as an effective insulin oral delivery method, the delivery system must comprise a biocompatible, high-loading platform affording insulin protection against external acidic environments and enzymatic degradation, in addition to targeted drug delivery coupled with a stimuli-responsive drug release such as hyperglycemia.

Nanocarriers such as polymeric, inorganic and solid-lipid nanoparticles have emerged as effective insulin transporters, circumventing many of the problems associated with insulin oral delivery. Those previously mentioned systems show promise for desirable biopharmaceutical and pharmacokinetic properties. However, recent clinical trials have resulted in failure of the nanoparticles due to toxicology, low levels of oral bioavailability and elevated intra-individual difference in insulin absorption – strong evidence that challenges still persist.

Two systems have, so far, been FDA approved for the oral delivery of insulin. The first one, developed by Oramed (ORMD-0801) incorporates both a species-specific protease inhibitor that protects active ingredients and a potent absorption enhancer that fosters their absorption across the intestinal epithelium. However, the system is non-specific and its prolonged use may damage the stomach membrane barrier and may lead to toxicity. The second, HDV-I by Diasome is based on liposomes with hepatic targeting, which suffers from instability in the GI tract, high cost and drug release during storage.

Q: How was the gastro-resistant nCOF prepared and tested in the latest study?

A: We developed nCOFs for glucose-responsive oral insulin delivery to overcome insulin oral delivery barriers. The insulin-loaded nCOFs exhibited insulin protection in digestive fluids as well as a glucose-responsive release, and this hyperglycemic release was confirmed *in vivo* using diabetic rats.

nCOFs feature a long-range ordered structure in which the organic building blocks are spatially controlled in two or three dimensions, leading to regular pores with diameters facilitating the loading and controlled release of large drugs and proteins/enzymes. In addition, their high flexibility in molecular architecture and functional design make them versatile and therefore give them unique responsivity to their environment.

Our technology has the potential to enable the oral delivery of insulin in a safer, more effective and patient-friendly manner; easing the treatment burden that is limited to intravenous or subcutaneous delivery.

In comparison to the two FDA-approved technologies, our system is biocompatible, highly stable in the stomach, cost effective, specific and glucose-responsive. It therefore represents a step forward in the future of insulin oral delivery and a novel pathway toward the treatment of Type I diabetes through nCOF-based insulin oral delivery.

Q: How does the nCOF nanoparticle method deliver the correct amount of insulin based on a subject's blood sugar levels?

A: In a hyperglycemic episode, the blood sugar level is high. The excess of sugar penetrates the nanoparticles and weakens the interactions between the insulin molecules and the nanoparticle framework, releasing them in the blood. The higher the concentration of blood glucose, the greater the quantity of insulin released. If the glucose level is normal, there is not enough sugar molecules to displace the insulin, which consequently remains within the nanoparticle, safe and protected.

Q: This study is preclinical. What will your next steps be in working towards human clinical trials of the technology?

A: The next step is to design and prepare a library of biocompatible nCOFs displaying high-loading insulin capacity and simultaneously affording insulin protection against the harsh conditions of the stomach, and a hyperglycemia-induced drug release mechanism.

Instead of using the trial-and-error method based on screening chemical space, which can be tedious, we will use computer-aided design. Candidates that are validated computationally for high performance will be synthesized and fully characterized in the laboratory. The COFs that show superior properties during loading and release, and simultaneously exhibiting a glucose-triggered release mechanism, will be selected as candidates for the *in vitro* and *in vivo* treatment of diabetes.

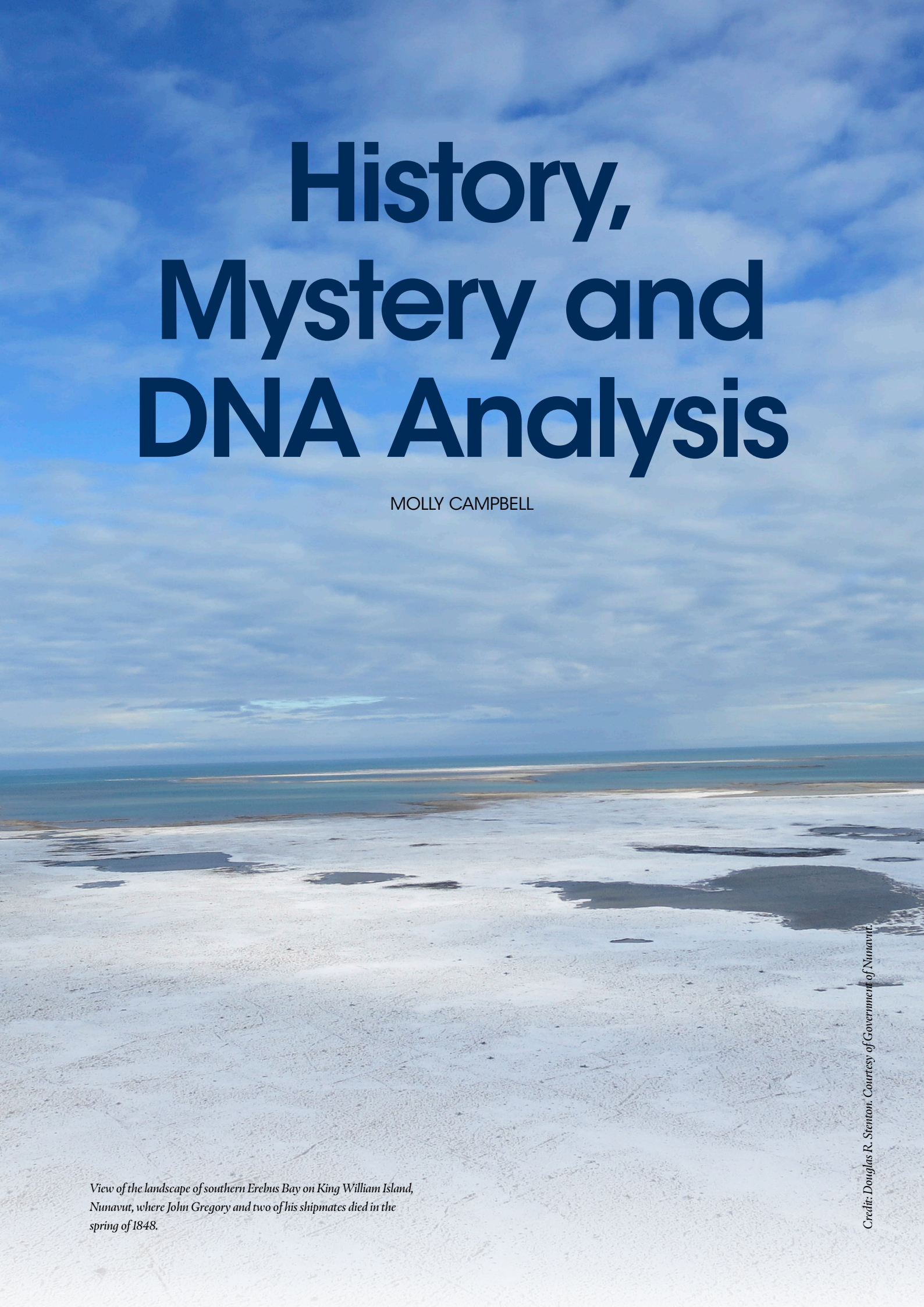
Q: Are there other diseases – in addition to diabetes – for which you expect the technology could be used to treat?

A: Our system could have a much wider use than insulin delivery; people with various health conditions may benefit from this new drug delivery method in the future. We envision a day in which a wide variety of biologics could be administered orally.

Antibodies could be delivered this way, or routine vaccinations if the device were loaded with antigens. In addition to the scientific significance of the proposed approach, the potential follow-up of the project would be the formulation of drugs against diseases of relevant social impact such as cancer, Alzheimer's and Parkinson's disease and dialysis-related amyloidosis. Within the UAE, such diseases are of particular concern and have become major public health issues. ●

History, Mystery and DNA Analysis

MOLLY CAMPBELL



View of the landscape of southern Erebus Bay on King William Island, Nunavut, where John Gregory and two of his shipmates died in the spring of 1848.

Credit: Douglas R. Stenton. Courtesy of Government of Nunavut.

The concept of identity, who we are and where we come from, has piqued human interest for thousands of years. The study of our origins, and those of our predecessors, is known as genealogy.

"Genealogy involves finding the relationships in your family and discovering who your ancestors are by using historical records and increasingly other resources to build up a story of your family," Else Churchill, a genealogist at the Society of Genealogists in London, explains.

Historically, it was considered to be a field of research concerned with aristocratic members of society – families with wealth, possessions, land or titles that could be claimed by subsequent generations. This viewpoint shifted gradually over time, Churchill emphasizes, as an antiquarian interest in family and community history evolved.

Birth, death and census records, diary entries, alumni associations, bar mitzvah records and oral histories are just some of the resources used by genealogists to trace lineages. The latter part of the 20th century saw the rise of computers, the internet and the digitalization of records – technological advances that bolstered the field by increasing access to such information. At a similar time, science was entering a revolutionary period – the "genomic era" – whereby advances in DNA analysis technology made it possible to sequence and analyze DNA quickly and at a low-cost. This progress gifted genealogists with a new, biological tool: DNA – the thread of nucleotides that tie us to our predecessors. And so, genetic genealogy, whereby DNA analysis is used to complement traditional genealogy methods, was born. It quickly became commercialized, and the first direct-to-consumer (DTC) genetic ancestry test was marketed in 2000.[1] By 2016, approximately 246 companies were offering online DNA tests, 30% of which were ancestry services, of some description.[2]

DNA analysis is a complement to the field, but it is not the whole picture, Churchill emphasizes: "Many people now might start their genealogy investigations with a DNA test but realize that to find details and more information they will have to use traditional methods too."

An incentive to using DNA for genealogical analyses is that it stands the test of time. Allentof *et al* calculated the half-life of DNA to be 521 years.[3] This means that after a period of 521 years, half of the bonds between the nucleotides of a DNA double helix would break. Fast-forward another 521 years, and half of the remaining bonds in *that* sample would have broken, and so on. Based on optimal preservation conditions, it would take 6.8 million years for every single bond in the DNA to break. New capabilities to extract "ancient" DNA are enabling scientists to understand the history of our planet and its inhabitants. Earlier this year, palaeogenetecists successfully extracted and sequenced DNA from a Siberian mammoth's molar. The DNA was estimated to be 1.2 million-years-old.

In terms of human genealogy research, the longevity of DNA means that, where the paper trail of history may not survive, DNA often will. It is helping academics and scholars to study and clarify our understanding of historical events in human history through bioarchaeological research. The most recent case study centers on the ill-fated Franklin Expedition.[4]

THE FRANKLIN EXPEDITION

In April 1845, British Royal Navy officer and explorer Captain Sir John Franklin departed from the shores of England with a crew of 129 men aboard two ships: HMS *Erebus* and HMS *Terror.* The explorers were assigned to search for a Northwest passage in the grueling conditions of the Canadian Arctic. In the years that followed, neither *Erebus* nor *Terror* returned to Britain.

In 1859, a rescue mission led by Francis Leopold McClintock was ordered by Franklin's wife. The team discovered a note in a cairn near Victory Point on the west coast of King William Island; it provided crucial information about what had happened to the voyagers. Early in the expedition (September 1846), the vessels became icebound in Victoria Strait, off the Northwest coast of King William Island, Nunavut. After being stranded for 18 months, the 105 surviving members of the crew chose to abandon the ships in late April 1848 as a last-ditch attempt at survival. By this point, Franklin himself had already passed away.

Sadly, their efforts were futile; every single member of the Franklin expedition would perish. Captured by the catastrophic event, historians, archaeologists and specialist investigators have puzzled over the explicit details of how and when the men died. "Much has been written about the expedition, from various perspectives, but we still have a limited understanding of what exactly happened," explains Canadian archaeologist Douglas Stenton, former director of Heritage for the Government of Nunavut Department of Culture and Heritage. "Various explanations for the expedition's fatal

Credit: Robert W. Park/ University of Waterloo.

Douglas Stenton excavating an as-yet unidentified sailor whose remains were found with those of John Gregory.

outcome have been advanced (e.g., lead poisoning, scurvy, botulism and tuberculosis, etc.), but the underlying causes are not well understood."

Skeletal remains have been found that were either known or presumed to belong to expedition members across a number of locations along the Western and Southern coasts of King William Island. While analysis of the skeletons can provide valuable insights, what remains elusive is the identities of the men; and so, 176 years after the ships left British shores, the interest in the expedition endures. "We know that at Erebus Bay, for example, at least 23 men died," Stenton says. What exactly happened there? Who were they? How many were officers, able seamen, or Royal Marines? "If that [information] was known, how might it affect current interpretations?" says Stenton.

Genetic genealogy brought a breakthrough in the Franklin expedition post-mortem in 2021. A small collection of bones discovered at Erebus Bay, on the Southwest coast of King William Island – approximately 80 km from where the ships became trapped – were identified as belonging to Warrant Officer John Gregory, an engineer aboard HMS *Erebus*, thanks to a DNA sample provided by a descendent.

Genealogical information suggested a five-generation paternal relationship, but would the DNA analysis confirm this?

Facial reconstruction of individual identified through DNA analysis as John Gregory, HMS Erebus.

Credit: Diana Trepkov/ University of Waterloo.

THE SEARCH COMMENCES

"The [King William Island] site has a fascinating history," explains Stenton. In 1859, the McClintock search expedition discovered the remains of two men in a small boat that had been hauled on a sledge by Franklin's men. They left the remains at the site, which were later discovered by Inuit. In 1879, a search expedition led by Frederick Schwatka rediscovered the site. The boat had been completely dismantled by Inuit to repurpose the wood and metal. Schwatka gathered the human remains together, buried them and erected a commemorative cairn over the grave. "At an unknown time, but likely in the 19th century, the cairn was dismantled, a few of the bones in the grave were displaced and the location of the grave became unknown," Stenton describes. "The site was rediscovered in 1993 by Barry Ranford and documented in 1994. In 1997, three displaced bones found on the surface were placed within a small cairn."

Stenton and his colleague Robert Park investigated the site in 2013, excavated the grave and collected the bones. They were sent to Trent University for osteological examination by Anne Keenleyside, who analyzed the remains to gather information relating to stature, age, sex and evidence of trauma or pathology. In 2014, the skeletons were returned to King William Island and placed in a new commemorative cairn. Prior to returning the skeletons – in an attempt to identify *who* the remains

belonged to – tooth and bone samples were sent to the Centre for Analytical Services Paleo-DNA Laboratory at Lakehead University for DNA analysis. Researchers in the lab extracted the DNA and performed feasibility tests that helped to determine which types of DNA were available for analysis. A profile was then made for each sample – some Y chromosome DNA (Y-DNA) profiles and all mitochondrial DNA (mtDNA) profiles.

mtDNA refers to our maternal ancestry. It is DNA that lies outside of the nucleus, in our mitochondria – organelles often nicknamed the "powerhouse" of a cell due to their role in energy conversion. mtDNA is passed down through the maternal lineage with very little mutation over time. It can be analyzed from both males and females to establish an unbroken maternal lineage.

Y-DNA, on the other hand, refers to paternal ancestry and is found using the Y-chromosome. "This type of DNA is passed down through the paternal (male) lineage with very little mutation over many generations. A father passes it onto his son," explains Stephen Fratpietro, technical manager at the Centre for Analytical Services Paleo-DNA Laboratory, and second author of the study.

Using the DNA profiles extracted from the samples, the researchers predicted which haplogroup – sometimes known as a "DNA signature" – they belonged to. Haplotypes are a set of markers, be it a combination of alleles or polymorphisms (variants), that are typically inherited together. "Since we now had a database of DNA profiles from the samples and [knew that] these types of DNA are passed on to successive generations, the next step was to find living descendants who would make good candidates for DNA comparison," says Fratpietro. The search commenced and would continue for several years with 16 failed matches.

FINALLY, A MATCH

In 2019, Jonathan – Joe – Gregory (38) of South Africa received a Facebook message from a cousin living in Canada. "It informed me that researchers [who had found skeletal remains] were reaching out to people around the world asking if they were prepared to submit DNA samples, predominantly from XY chromosome males," he says.

Joe recalls "always having an awareness" that a connection between his family and the Franklin expedition may exist, but it had not been conclusively determined. Genealogical information suggested a five-generation paternal relationship, but would the DNA analysis confirm this?

Joe provided a buccal swab to the team for DNA comparison. Transportation issues, coupled with the disruption caused by the COVID-19 global pandemic, meant the line of communication went quiet for a short while.

For the Gregory family, the discovery is not an obituary, it is history.

Left: Stuart Gregory. Right: Jonathan "Joe" Gregory. Front: Owen and Adam Gregory.

Credit: Joe Gregory.

Artifacts belonging to Edward John Gregory, now in possession of Joe Gregory.

Meanwhile in the lab, Fratpietro and team were constructing a Y-chromosome profile from Joe's DNA. This was not an easy feat due to the level of preservation of the samples from the Franklin expedition. Not all of the samples submitted for analysis yielded both mtDNA and Y-DNA for profiling. "A lot [of the samples] only contained mtDNA. In terms of finding living descendants, Y-DNA is easier to trace back to a member of the Franklin Expedition using genealogy because a last name is usually passed on to the male children. Tracing back one's roots using mtDNA is a bit more complicated since it is traced back through the female lineage," Fratpietro says.

The team found a match of 20 markers from Joe's profile to a 20-marker profile from a sample labeled NgLj-3:34. Based on Joe's lineage information, the researchers hypothesized that the excavated DNA sample belonged to Warrant Officer John Gregory.

The significance of the match had to be verified, and so the profile was compared to a Y-chromosome database to calculate its frequency. In a database of 73,006 other profiles, it was unique, Fratpietro explains: "Additionally, we performed another calculation to determine the kinship index, which is a likelihood ratio of someone being paternally related versus not being paternally related. That index was 47,030 – such a large number that it would indicate strong support that Joe and NgLj-3:34 are 47,030 times more likely to be paternally related than unrelated."

NgLj-3:34 was John Gregory, and Joe Gregory is his great-great-great-grandson.

A TWIST IN THE TALE

Joe was informed of the news via email, and recalls having to hold on to the edge of his seat as the word "match" appeared in the subject line. "There's a link now, and we can relate to it on so many levels," he delights.

Stenton, Fratpietro and colleagues sought the services of a professional genealogist in Britain to conduct archival and database research in order to clarify what was known about John Gregory. He was married to Hannah Wilson and they had a son, Edward John Gregory. Prior to the expedition, he worked as an engineer for a marine steam engine firm in Lambeth, London. Based on available records, it would appear that John was hired for the voyage at short notice and was compensated with an increased salary. In 1845 he wrote to Hannah. In the letter, he spoke of spotting icebergs and whales in Greenland, verifying that the voyage had not yet reached the Canadian Arctic. Hannah never heard from John again.

In 1850, Edward Gregory had a son that bore the same name: Edward John Gregory – the famed British artist that commissioned the Boulters Lock painting. While not mentioned in the study publication, Joe is in possession of several artifacts worn by Edward, including a waist coat and an original version of the famed painting.

AN "IMPORTANT COMPONENT" OF BIOARCHAEOLOGICAL RESEARCH

This is just one example of a historical case solved using genetic genealogical methods, and it is likely there will be many more to come in the future. Stenton believes it is a "fascinating approach": "Its potential has been demonstrated in many archaeological contexts, and it has become an important component of bioarchaeological research," he says.

For the Gregory family, the discovery is not an obituary, it is history. They express sheer gratitude to the researchers for unlocking this vital information regarding their families' origin that has been frozen in time.

The researchers encourage any individuals that believe they could be living descendants of members of the expedition to come forward, so that they continue their quest of identifying the voyagers' remains using DNA analysis. ●

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Credit: Joe Gregory.

TECHNOLOGY NETWORKS

PHARMACOGENOMICS

Over recent years, the medical field has placed increasing focus on making personalized medicine, whereby our medical treatment plans are tailored to us as individuals, more mainstream across the globe.

A key area of personalized medicine is pharmacology. Many marketed drugs are prescribed by medical professionals as a "one size fits all" medication. However, these medications can actually elicit different effects in different people.

The field of pharmacogenomics explores the role of the entire human genome and epigenetics in determining an individual's drug response.

To learn more, access the full infographic here

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Unintended Consequences: The Risks of Vacating COVID-19 Vaccine Patents

MICHAEL S. KINCH

The following article is an opinion piece written by Michael S Kinch. The views and opinions expressed in this article are those of the author and do not necessarily reflect the official position of Technology Networks.

Last month, my co-author and I published a book on the history of drug pricing in recognition that an inability to pay for medicines is growing into a public health emergency, with the potential to be every bit as dangerous as the current pandemic. Nearly 40% of respondents claimed to have skipped medicines due to solely to cost. Public opinion in the US seems to be reaching a tipping point, where it seems likely that government intervention will be necessary to guarantee access to vital medicines.

Although the publisher elected to name the book, *The Price of Health*, we originally wrote a manuscript titled, *Unintended Consequences*. This concept captures the fact that runaway drug prices are largely a consequence of unforeseen problems arising from well-intended actions. This insight provides an important cautionary tale that is relevant to the news of today.

In researching this book, we learned that aggressive and sometimes abusive deployment of patents by the pharmaceutical industry contributes to high prices. We were hardly the first to state that the intellectual property system needs to be reviewed and likely reformed. As we do so, we must carefully consider the use of both incentives (carrots) and discouragements (sticks) in a manner that incentivizes the discovery of new medicines while assuring these will be widely available.

With this in mind, I was deeply troubled at the recent stance by the Biden

administration that it would undermine or eliminate patent protection for COVID-19 vaccines.

This seeming inconsistency (given patents contribute to high prices) can be squared by referencing a 2018 book I composed about the history of vaccines. It is commonly stated that vaccines have saved more human lives than any other human invention, other than perhaps clean water. The title of this book, *Between Hope and Fear,* reflects two antithetical views of vaccines as perceived by the some in the public (e.g., anti-vaxxers) and views from the board rooms of many pharmaceutical companies.

Amidst relating the wonders of vaccines that eradicated scourges that had plagued our species from time immemorial, I pointed out a concerning trend revealed by scientific research published by the Center for Research Innovation in Biotechnology at Washington University in St Louis. In brief, the number of vaccine-preventable infectious agents has remained largely stagnant since the 1990s. Likewise, the number of companies performing research and development on novel vaccines has decreased, with comparatively few companies remaining actively engaged in the discovery of vaccines against pathogens.These declines reflect neither a victory in our war against long-standing nemeses (e.g., pandemic forms of influenza, tuberculosis or malaria) nor a lack of newly-discovered microbes that can cause death and disease (e.g., Ebola, Zika and of course, coronaviruses such as SARS or MERS). Rather, the financial attraction (or lack thereof) of vaccines to the pharmaceutical industry pales in comparison with more lucrative markets, most notably cancer. Whereas insurance companies and consumers have become seemingly desensitized to six- or seven-digit price tags for new oncology drugs, a very different view prevails for vaccines. Yet a price tag of a few hundred dollars for Gardasil was sufficient to trigger considerable criticism. As a consequence of such experiences, many companies did the math and elected to decrease their exposure to, or walk away altogether from, vaccine research and development for infectious diseases. Much of the immunology expertise that had been devoted to infectious disease vaccines was instead redirected to the discovery of new cancer medicines, which could be offered at much higher prices.

It is no coincidence that most of the companies that have been rightfully praised for innovative mRNA vaccines (Moderna and BioNTech), were mostly focused upon oncology products prior to the pandemic. Cancer predominated despite the fact that mRNA technology held great potential to address both established and emerging infectious agents, from malaria to Dengue fever.

Most importantly, these technologies could offer a potential for a universal influenza vaccine to prevent periodic (and inevitable) recurrences of pandemic influenza viruses. For example, the H5N1 and H7N9 strains of influenza may have mortality rates in excess of 50%. Though controversies rage around this rate, even the low estimates eclipse even the worst imagined strains of SARS-CoV-2. Such a calamity might still be averted were we to build upon the momentum and learnings of the COVID-19 vaccine development.

sequences of a premature or arbitrary undermining this system could have lasting repercussions.

A dynamic and nimble patent system was described in Section 1, article 8 of the United States Constitution itself. This forward-looking approach allowed the United States to become and remain the world's leading innovator since the foundation of the nation. Yet, this position looks increasingly fragile and relies upon

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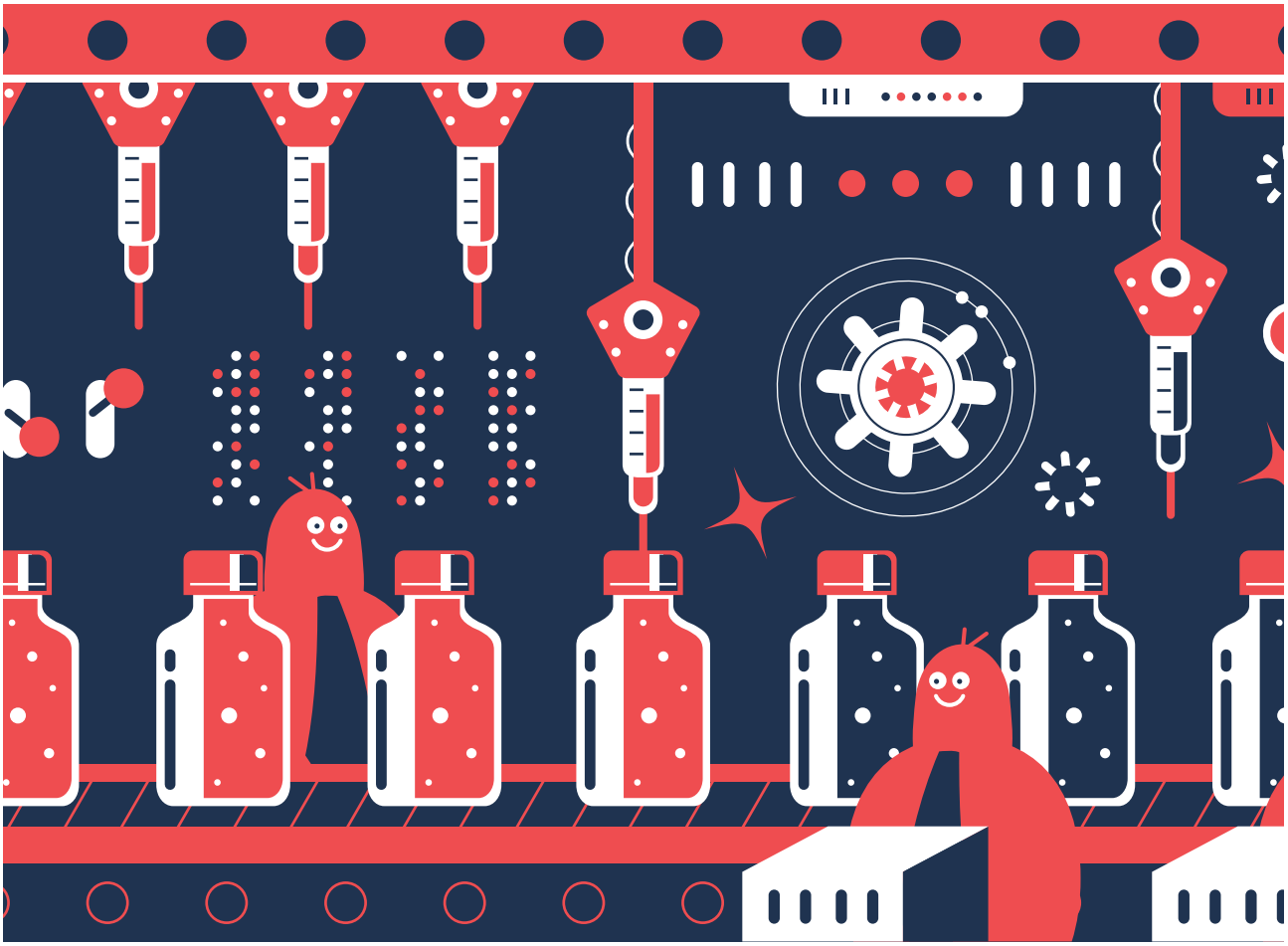
The announcement that the United States might waive intellectual property rights could stymie the discovery and deployment of new vaccines; returning us to the same vulnerable position we occupied in the closing days of 2019. All the wiser and yet, somehow, not. While I remain firmly in the camp that the patent system needs to be updated and reformed, we must appreciate that patents do indeed provide an incentive for innovation. The unintended consequences of a premature or arbitrary undermining this system could have lasting repercussions.

A dynamic and nimble patent system was described in Section 1, article 8 of the United States Constitution itself. This forward-looking approach allowed the United States to become and remain the world's leading innovator since the foundation of the nation. Yet, this position looks increasingly fragile and relies upon public trust in intellectual property. The well-intended acts to waive patent rights for COVID-19 vaccines could have the unintentional consequence of squashing the development of future vaccines. There is no question that the patent system needs to be cleansed of abuse but we must do so in a manner that properly balances incentives and discouragement (carrots and sticks). Most importantly, we should take the time to consider the impact of unintended consequences.●



Vaccine Production: Navigating Scale-Up Challenges

PRIYOM BOSE

The ongoing COVID-19 pandemic is caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and has claimed over 3.1 million lives worldwide. It has also had a humongous impact on the global economy. Limited success in designing new drugs and repurposing existing drugs to treat COVID-19, has led to a research focus on preventives, which includes vaccines. Thereby, many researchers are working at record speed to develop COVID-19 vaccines, and to date, many new vaccines have received emergency use authorization (EUA) from global regulatory bodies, such as the US Food and Drug Administration (FDA), the Medicines and Healthcare products Regulatory Agency (MHRA) and the European Medicines Agency (EMA).

After a new vaccine is designed, the main challenge that the manufacturers face is scaling up its production. In the current situation, an added challenge is achieving large-scale production at a rapid pace. Although pharmaceutical companies have been able to manufacture hundreds of millions of doses of COVID-19 vaccines in a short period, demand continues to increase. To vaccinate the global population, the world needs billions of vaccine doses, quickly. The transition from manufacturing vaccines in smaller quantities required for academic research to the mass production that is required to protect the global population can be a daunting task.

CHALLENGES IN THE LARGE-SCALE PRODUCTION OF VACCINES

Typically, more than 200 individual components are required for the production of a vaccine. These components, such as glass vials, syringes, filters, tubing, stabilizing agents and disposable bags, are often produced in different countries. In a summit of manufacturers and policymakers, Richard Hatchett, chief executive of the Coalition for Epidem-

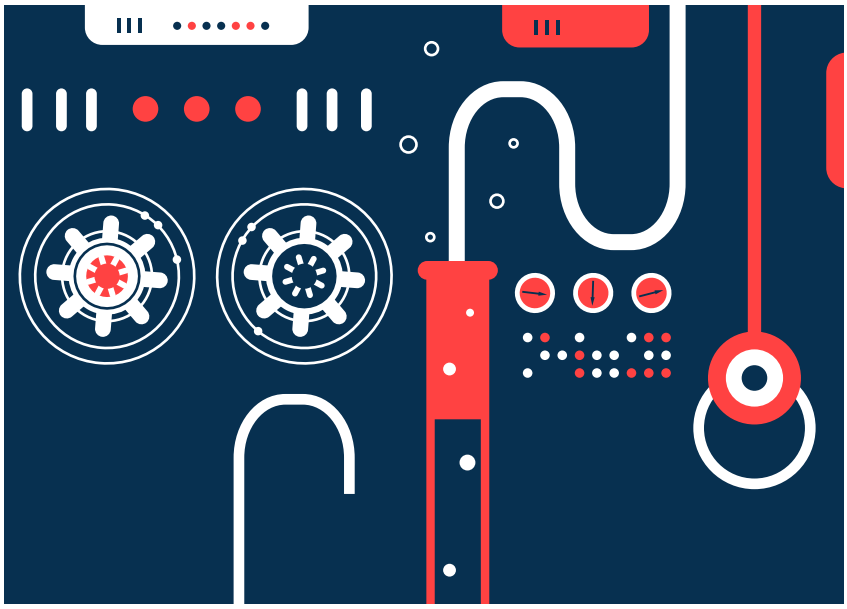
ic Preparedness Innovations, pointed out that if the supply of one of the components falls short, the production of the vaccine can be delayed. According to Duke University's Andrea Taylor, leader of global innovation programs on evaluation, scaling and adaptation of healthcare innovations to address critical access and quality challenges, a break in the supply chain can occur owing to various reasons, such as the exporting countries threatening to block vaccine component shipments. Such an incident occurred recently when India and the European Union announced restrictions on vaccine exports. Before the ongoing COVID-19 pandemic, there was a lack of established networks of contract manufacturers. This problem was further exacerbated owing to the massive global demand for large-scale production of vaccines currently.

Scientists believe that the large-scale production of COVID-19 vaccines is limited owing to the highly concentrated state of global vaccine manufacturing capacity. At present, very few countries have the domestic capacity to manufacture COVID-19 vaccines. "Scaling up vaccine production is challenging and the lack of sufficient manufacturing plants is hampering the global vaccine supply," said Zoltán Kis, a chemical engineer at the Future Vaccine Manufacturing Hub at Imperial College London. Kis' expertise lies in the area of vaccine manufacturing; he works to design novel technologies capable of producing large amounts of vaccines against known and unknown pathogens. More recently, he has been focused on COVID-19 vaccine production processes based on rapid-response technologies, such as the RNA vaccine platform.

"There is a lack of optimization at various stages of manufacturing for two key reasons, because these are newly designed vaccines and because they have been developed in such a short timeframe,"

— KIS

Dr Kis further said that "there is a lack of optimization at various stages of manufacturing for two key reasons, because these are newly designed vaccines and because they have been developed in such a short timeframe. However, this limitation is expected to be mitigated as manufacturers become more familiar with each vaccine and as processes are optimized."



Another key challenge is to develop vaccines that are affordable to low- and middle-income countries (LMICs). Several companies, such as AstraZeneca and Johnson & Johnson, which rely on public-sector investments, have claimed to sell their vaccine globally at a low cost during the pandemic to improve accessibility. However, the cost of vaccines, post-pandemic, is yet to be determined.

OVERCOMING KEY CHALLENGES RELATED TO VACCINE SCALE UP

As outlined in a special report published in *Nature*, researchers explain that to accelerate vaccine production, collaboration is extremely important. It is essential to collaborate with multiple supply partners and analytical testing sites, in different countries. Recently, Martin Friede, head of vaccine development at the World Health Organization (WHO) stated that WHO has identified several organizations worldwide and is providing matchmaking services by connecting producers of vaccine components and major manufacturing companies. One of the world's leading companies in the area, AstraZeneca, has collaborated with multiple manufacturing facilities across the world to support each stage of production. The manufacturing processes are transferred to the respective facilities and each of these facilities is governed and technically guided, throughout the manufacturing process, by the "parent" company.

Widespread transfer of technology and data across manufacturers, around the world, is vital when there are pressing challenges related to scaling up vaccine production. In the current COVID-19 pandemic, many vaccine manufacturing companies have united to cater to the global

demand for vaccines and this initiative should actively continue.

In many organizations, across multiple industries, data sharing remains a key issue – and pharma is no exception. This lack of transparency can lead to the generation of data silos. An isolated approach to data storage can have several disadvantages, for example, it can lead to a duplication of work effort, slows down data analysis and can stunt innovation. Besides clinical trial data on vaccine candidates, epidemiological modeling studies and reports on monoclonal antibodies should be shared widely among biopharmaceutical companies in advanced countries as well as LMICs.

Intensifying the process of vaccines and biologics production, in terms of its magnitude, may play a key role in making vaccines affordable

The pharmaceutical industry is recognizing the importance of "connecting" siloed data and is taking steps towards solving the problem.

The WHO and its partners have undertaken an initiative to bolster the vaccine production capability of LMICs by establishing a multiple technology transfer hub. The main aim of this initiative is to provide training and knowhow, to interested companies in LMICs, regarding mRNA vaccine technology. In the future, the plan is to extend this technology transfer to other vaccine development processes.

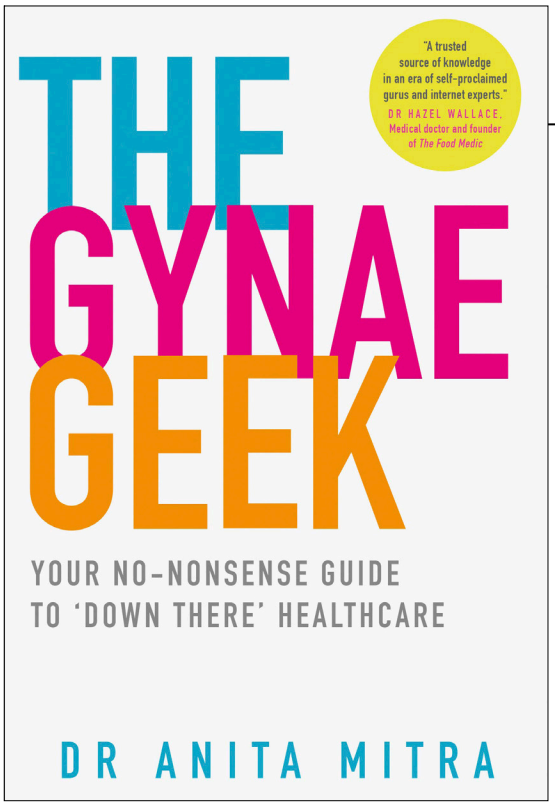
For scaling up vaccine production, developers have enlisted 53 manufacturing sites in Europe. This number

is gradually increasing as more partnerships are being formed between vaccine developers and manufacturing organizations. Kis stated that "increasing the number of manufacturing plants is one of the most effective ways to increase vaccine production and meet the global demand." However, scientists are wary that a diversion of resources to developing COVID-19 vaccines may hamper the production of vaccines for other diseases, such as cancer.

Optimization and quality checking is another area that can help in bringing about a rapid increase in the scale of vaccine manufacturing. Environmental conditions, such as heat, light and radiation, can affect the quality and purity of vaccines. Different technologies are being used to evaluate vaccine quality. For example, polymerase chain reaction (PCR) is used to analyze the adenoviral vector that carries the spike protein's genetic code and the viral titer is measured using high-performance liquid chromatography (HPLC). HPLC helps to remove multiple contaminants from *in vitro*-transcribed RNA and eliminates immunogenicity. While there are several approaches that can be employed to ensure purity, anion exchange chromatography (AEX) is typically the most widely used. This is because the isoelectric point of the majority of viruses is below six. Owing to this property, the viruses can efficiently attach themselves to anion exchange matrixes at neutral pH. The separation of viruses, from impurities, is brought about by selective elution, because many impurities also bind to the anion exchangers at neutral pH. The use of affinity chromatography in vaccine purification helps to enhance the yield and analyze the purity of the vaccine. This technique also helps in reducing numbers of downstream process operations. Researchers will continue to assess and refine storage and handling conditions, at each phase of the vaccine production, to ensure stability, shelf life and safety. In the current scenario where production rate is extremely high, quality and stability testing are being carried out simultaneously with the manufacturing process.

As mentioned earlier, large-scale manufacturing of affordable vaccines is a challenge. According to Martin Friede, intensifying the process of vaccines and biologics production, in terms of its magnitude, may play a key role in making vaccines affordable. This might also have positive spillovers to other vaccines. While the COVID-19 pandemic has provided strain to existing production processes, in the process of meeting the unprecedented demand for vaccines, manufacturers have had the opportunity to innovate and streamline vaccine production on a large scale. Such optimization may yield rich dividends in the future regarding the manufacture vaccines more broadly. ●

Science in the Media



THE GYNAE GEEK

BOOK BY ANITA MITRA

Did you know that the fallopian tubes can pick an egg from either ovary? Have you ever wondered if intense period pain is normal? Well, this book will help you find out.

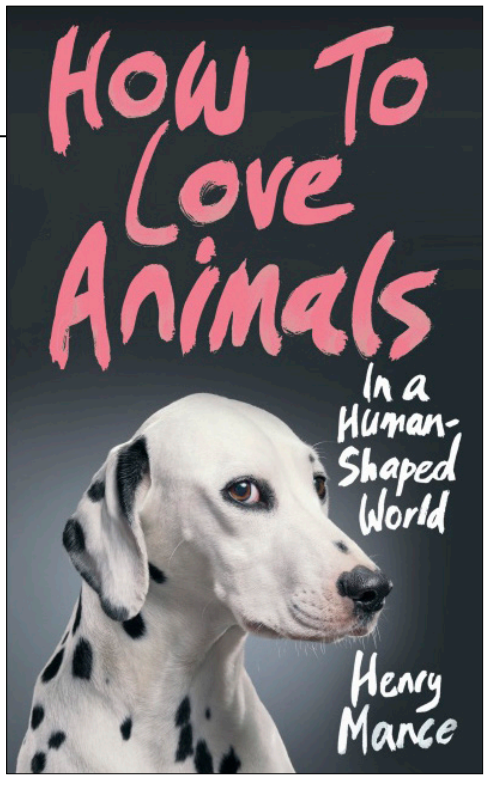
Dr Anita Mitra is an NHS doctor based in London working in obstetrics and gynaecology with a large Instagram following. This book takes you on a journey from the first period to the onset of menopause, whilst offering reassuring and open-minded advice.

I listened to it as an audiobook (voiced by the author herself) on my drive to my family's house. Throughout that time, I was suspended in intrigue and hilarity, as I learnt more from this book than all previous sex education. Since reading *The Gynae Geek*, I have recommended it intensely to many of my friends and family (male and female alike) and I will continue to do so.

Beccy Corkill

HOW TO LOVE ANIMALS: IN A HUMAN SHAPED WORLD

BOOK BY HENRY MANCE

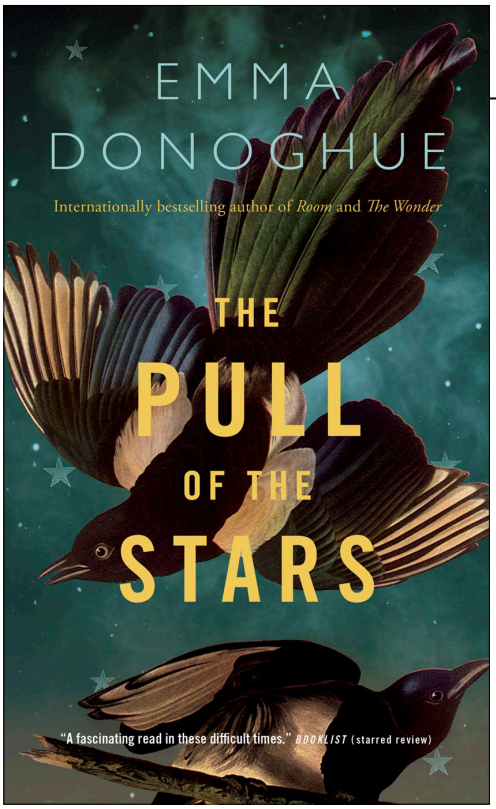


If we took animals' experiences seriously – how would we eat, think and live differently? For me, this is an urgent and thoroughly engaging exploration of our relationship with animals. If we appreciate animals on holiday, in birthday cards and in wildlife documentaries, we can't just cover our eyes and ears to farming and extinction.

Henry Mance sets out on a personal quest to see if there is a fairer way to live alongside animals in a provocative, witty and sometimes brutal consideration of the inconsistencies in how we treat other species. He explores the dilemmas around hunting, overfishing the seas, visiting zoos and owning pets.

He began the book as a vegetarian and is now, as a result of his research, a vegan – despite his wife (a vegetarian) warning him: "It's divorceable". This isn't a book about what animals can do for us, but a book about what we can do for them.

Lucy Lawrence



THE PULL OF THE STARS

BOOK BY EMMA DONOGHUE

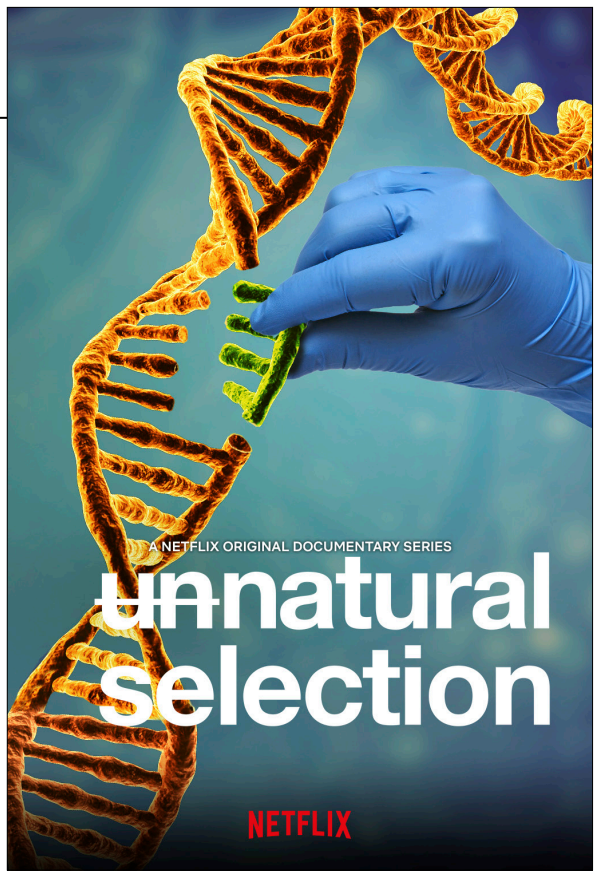
"We could always blame the stars."
"I beg your pardon, Doctor?"
"That's what influenza means: influenza delle stelle – the influence of the stars."

Immersing yourself in the devastation of a historic pandemic whilst living in a contemporary one might be all too much at this timepoint. However, if you can, I urge you to pick up a copy of this book by Irish-Canadian playwright Emma Donoghue. *The Pull of the Stars* transports us to 1918 Ireland, in the midst of the influenza pandemic. Nurse Julia Power, our protagonist, is working on a maternity fever ward in an under-staffed and overburdened hospital in Dublin. Patients admitted to the ward with "the grippe" are experiencing pregnancy complications that dumbfound even the most highly qualified hospital staff. Over the course of just a few days, the novel explores the tireless efforts of nurse Power and her comrades – doctor Kathleen Lynn and orderly Bridie – to save the lives of their patients, and to heal the wounds they bear from living in a society that has not been kind to them. It is a story of loss, humility and opening to new beginnings amidst times of hardship.

Molly Campbell

UNNATURAL SELECTION

DOCUMENTARY, NETFLIX



Unnatural Selection is a fascinating – and at times unnerving – four-part docuseries that explores various genetic engineering techniques and their impact on our society and the environment.

The polarity caused by the advent of the CRISPR-Cas9 genome-editing technology is captured well by film-makers Joe Egender and Leeor Kaufman, as they follow the struggles of individuals suffering with various genetic disorders. Though it is difficult to deny the impact of gene therapy on many of these individuals' lives, these emotional scenes are offset against valid concerns from scientists, bioethicists and environmentalists about the consequences of the technology's uncontrolled use.

Whether you have an interest in genetic engineering or are completely new to the topic, this series is guaranteed to make your head spin and evoke some important yet controversial questions...

Tiffany Quinn


TECHNOLOGY NETWORKS
TN
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No I haven't. Could you tell me more?
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Our Facebook groups allow you to keep up to date with the latest news and research and share content with like-minded professionals. With three diverse groups there is something for everyone.
Sounds great! How do I join?
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nnr
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ACT
Discover the Analytical Chemistry Techniques Group here.
TSE
Explore The Science Explorer Group here.
Thanks! I'll come join the conversation. 👍
Aa