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UOA

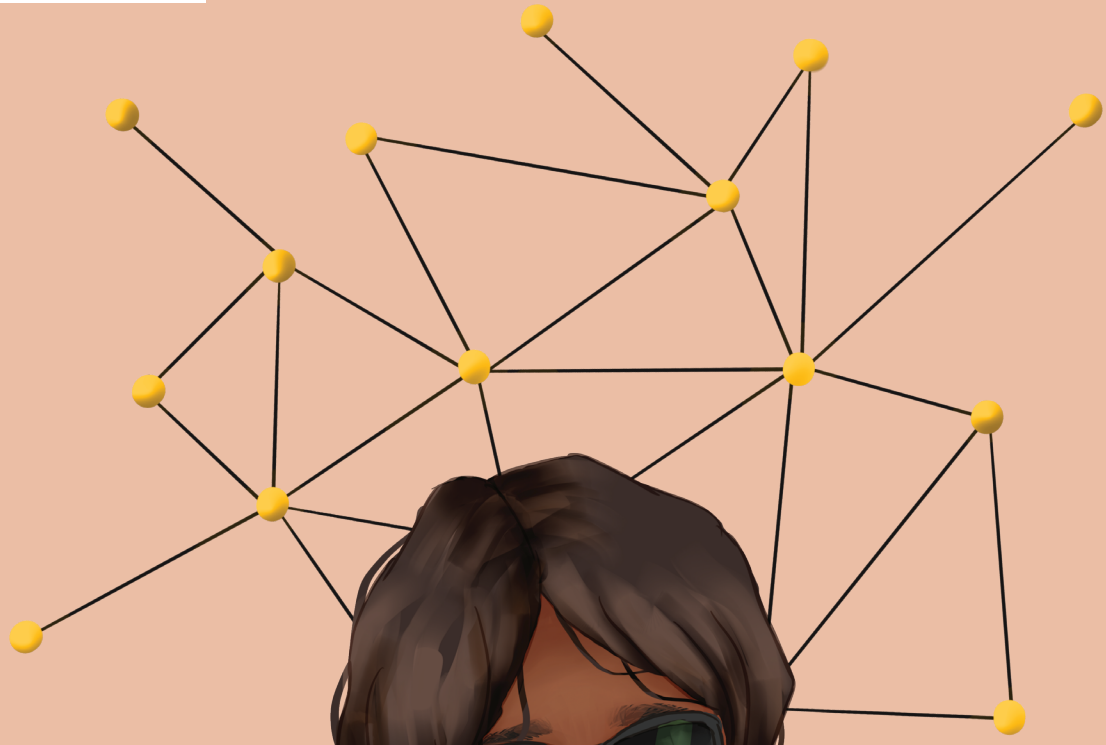
Scientific

A student-run publication

13 Are AIs Smarter than a 5th Grader?

A review of recent developments toward solving the Math Word Problem

Computer Science



Editors' Note

Welcome to the first issue of Volume Two of the University of Auckland *Scientific*.

As the mid-semester break ends, many of you will have spent some well-deserved time off from lectures and tutorials. Many students will have finished off assignments and other academic projects. The executive team at UoA Scientific are proud to release the first issue of Volume Two of the University of Auckland *Scientific*.

With Volume Two, we hope to improve upon the quality of the magazine by inviting postgraduate students and other academics to peer review our articles. It is of utmost importance to us that our articles remain scientifically accurate and that we retain the integrity of our publication. For this edition, the article '*Pinpointing Breast Cancer from a Bioengineering Perspective*' has been edited by bioengineering Research Fellow Thiranja Babarenda Gamage. Another exciting addition to this issue was the incorporation of original artwork by our marketing coordinator Aimee, for our front cover.

As always, we continue to strive to engage with the community of scientific readers, this year by expanding our distribution locations across campus. New distribution sites include Grafton Hall, Carlaw student village, the Faculty of Engineering Building, and the Kate Edger Building. We will also continue to distribute copies of our magazine on several levels of the Science Centre for you to enjoy!

For Issue One, we have brand new guest writers from a large range of academic disciplines. Our cover article on this issue features writer Anne Newmarch, who discusses solving the Maths Word Problem with machine learning models. Our other talented guest writers included Lucas Tan, whose article talks about the ethical boundaries of the gene-editing tool CRISPR. Max Dang Vu shares his own research which highlights the challenges of breast cancer diagnosis and discusses novel biomechanical techniques to resolve these issues. Moving away from the discipline of bioengineering, Sheeta Mo considers to what extent science fiction novels represent true science in the context of psychology. Caleb Todd returns with his second article of the series 'Einstein's Year of Miracles'. The second instalment is titled - *Part Two: Atoms*.

In addition to our guest writers, three writers from our executive team have contributed fascinating articles for this issue. Marketing coordinator Aimee asks the question: 'How do stars age?' and explains the Algol paradox. Creative director Gene discusses his summer research project about assessing the quality of retinotopic mapping with connective field modelling. Finally, secretary Jasmine explores the undesirable organisms of the world, and why they are important to their respective native ecosystems.

Before we wrap up the editors' note, we would like to acknowledge a few individuals who allowed for the creation of this issue. We would first like to thank Vanessa Hefer (Communications and Marketing Manager of the Faculty of Science) for diligently answering our questions and allowing us to liaise with the Science Faculty. Next, we would like to thank Holly Honeysett (Student Academic Adviser) for assisting us with finding guest writers for the magazine. We would also like to thank all the guest writers in this issue for their amazing work! And as always, thank you to our readers. We are so grateful to be able to reach those passionate about science with our publication.

We hope you enjoy reading this issue as much as we did!

Ngā mihi,
Jasmine Gunton, Secretary for UoA Scientific 2022

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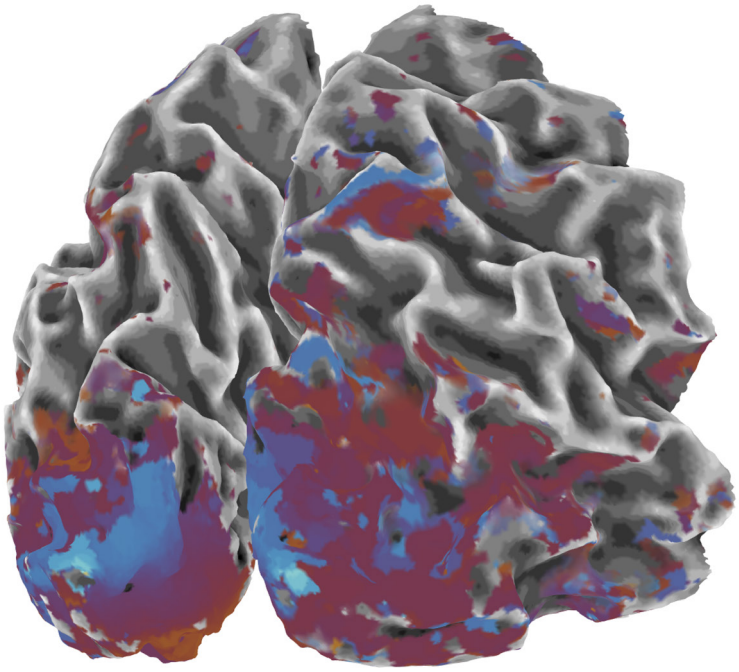
Assessing The Quality of Retinotopic Maps Derived From Functional Connectivity

Gene Tang



To many of us, visual perception seems to be rather effortless, but in reality, our brain processes a plethora of visual phenomena consistently and endlessly. Our perception starts with our neural mechanism transducing electromagnetic energy into action potentials. The distant world we see is translated into a proximal stimulus that impinges on our retina, and that information is subsequently mapped onto our brain. The mapping of the retinal visual input to the neurons is known as retinotopy. This field of study has opened us to opportunities to understand how our visual information is organised in the brain [1]. The simple notion of the retinotopic mapping is that the adjacent locations on visual space are represented by adjacent neurons in the cortex. In saying that, the representation is not exactly a mirror-image. Our visual image is represented contralaterally on our visual cortex with the left side of the visual field projecting onto the right hemisphere, and vice versa. The upper visual field is also represented in the lower side of the visual cortex, and vice versa.

Functional magnetic resonance imaging (fMRI) provides us with just a channel to observe this cortical organisation of the visual world. The introduction of an fMRI method, known as the population receptive field estimates (pRF), provides us with a method in visual field mapping [2-3]. The pRF maps visual topology by determining the brain voxels that produce the largest response to a particular position in the visual field [2]. Here, we won't go into much detail about the conventional pRF mapping but please do keep an eye on our next edition.

It would be valid to say that the pRF method proposed by Dumoulin & Wandell in 2008 [2] has set a gold standard, or ground truth, in human retinotopic mapping. pRF has been popularised as it was proven to be very successful in several ways, ranging from investigating the organisation of the visual cortex to examining plasticity and cortical reorganisation of patients [4-5]. However, despite the robustness of the pRF, there are still some limitations to it. Concerns may lie with possible confounding variables that manifest during the long scanning session. As the subjects are required to fixate at a single spot, watching monotonous stimuli (such as a checkerboard), factors such as the patient's medical condition, comfort, and exhaustion can all affect their ability to properly complete the task, thus affecting the results.

Fortunately, a novel technique called connective field (CF) modeling [6] has provided us with a promising method for visual field mapping and analysis, with fewer constraints than ever before. By using the same set of data, instead of determining the correlation between the largest brain response to a location in the visual field, CF modeling quantifies responses of the different brain regions that coincide with the responses in the primary visual cortex, which is also known as V1 [6]. Using a template of how the V1 represents the visual field, we can then translate the peak correlation in V1 into a prediction of other locations of the visual field that maps onto a given location in the brain. As the response is now identified in terms of the inter-areal activations rather than the correspondence between the position on the visual field and on our visual cortex, this method can theoretically liberate us from the previous requirements of steady fixation and controlled

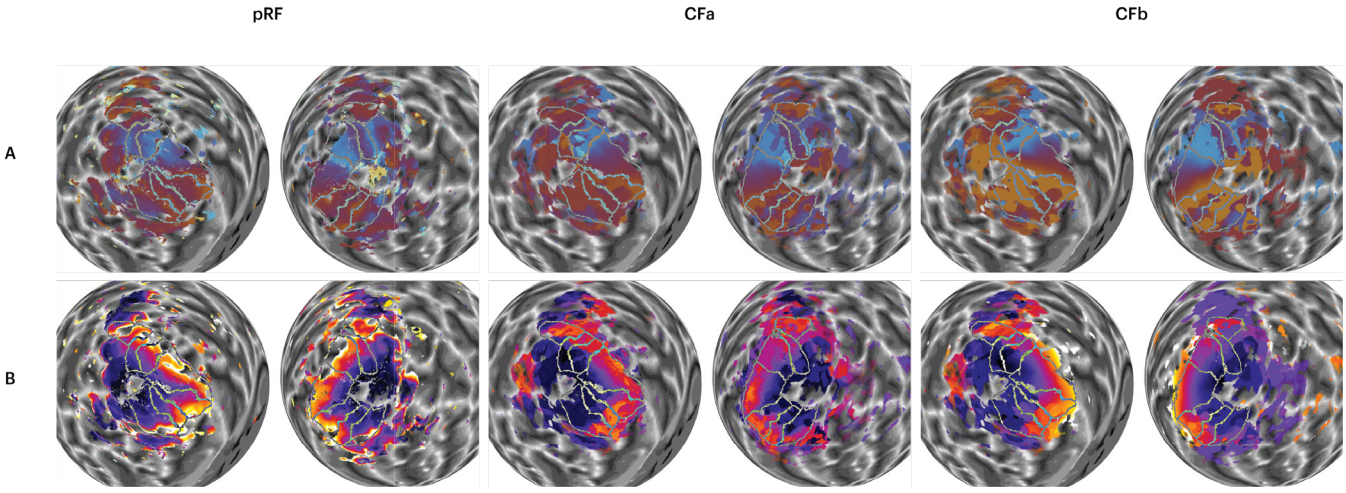


Figure 1: Visual field maps derived from the pRF and CF method. Polar angle maps (A) and eccentricity maps (B) on a spherical model of the two cortical hemispheres. Table of polar angle and eccentricity maps of a subject comparing the visual field maps derived from the pRF (left), CFa (middle) and CFb (right).

stimuli. Instead, subjects can freely view movies and naturally move or even close their eyes [7]. The subject's activity measured inside their V1 should thus yield adequate information necessary for retinotopic mapping.

During the summer, Assoc. Prof. Sam Schwarzkopf and I conducted research to assess the quality of the retinotopic maps derived from the CF method. We used the fMRI data previously collected from 25 subjects by Dr. Catherine Morgan and Prof. Steven Dakin. First, we analysed the data using the conventional pRF method. Then, we delineated the visual regions from both hemispheres of all the subjects using SamSrf software (visual field maps delineation can simply be understood as the tracing of the visual area borders based on the fMRI renders). The delineated regions were later also applied to the maps generated by the CF method. After that, we compared the pRF and CF map side-by-side, and qualitatively analysed the similarities and differences between the two methods. What happened after our first qualitative analysis was that we recognised that there were a few constraints that came with our original CF map derived from a group average template (hereafter referred to as CFa), so we included another CF template based on the probabilistic prediction of the cortical anatomy alone (hereafter referred to as CFb) [8]. Ultimately, we carried out statistical inference to investigate the difference between these three maps (pRF, CFa, and CFb) in terms of their coverage (the proportion of vertices in the occipital lobe that passed $R^2 > 0.01$ threshold), angular and eccentricity[1] correlation, and similarity (quantified by the mean Euclidean distance between pRFs in the maps).

Our Results

We first began with the qualitative analysis of the data. Initially, we compared the CFa map and pRF map side-by-side. Figure 1 shows example maps of a subject. Here, we summarise our observations between the maps derived from the two methods. Firstly, the CFa map appears to have greater coverage than the pRF map. This is particularly true in higher visual areas such as the V3B, LO, and MT. However, CF maps are generally cruder than the pRF maps, especially as pRF represents polar angle and eccentricity with smoother gradients. For polar angle, this means that maps based on CF (with either template) would be harder to delineate. Not only are the CF maps overall cruder, the borders of V2 and V3 in the CF maps appear to be clearer in dorsal (lower) areas, but less noticeable in the ventral (upper) areas. Borders of other areas such as V3A, V3B, and V4 also appear to be much weaker in the CF maps. For eccentricity maps, CFa appears to show a reversal around the medial borders where the peripheral edge should be with maximum eccentricity being lower than in the pRF maps. This is because of a statistical artefact when using a group average. The idea here is that, as the template is based on the group average, the mapping of eccentricity beyond the group average tends to be restricted. The probabilistic template used for CFb maps can thus overcome this issue.

Next, we quantified the differences between the groups in terms of coverage, polar/angular correlation, eccentricity correlation, and the Euclidean distance. We wanted to be sure that any differences noticed in the qualitative analysis weren't due to our own subjective judgement. The results are shown in Figure 2. To assess the coverage differences between three groups (Figure 2A), we conducted a non-parametric ANOVA. We found that coverage for pRF maps was significantly lower than for CF maps. This difference was observed across all vertices (the data points across the brain template) that passed the set threshold, as well as separately in all individual regions. To put it another way, we

[1] Polar angle/angular and eccentricity are the two crucial orthogonal dimensions required to identify locations in the visual space.

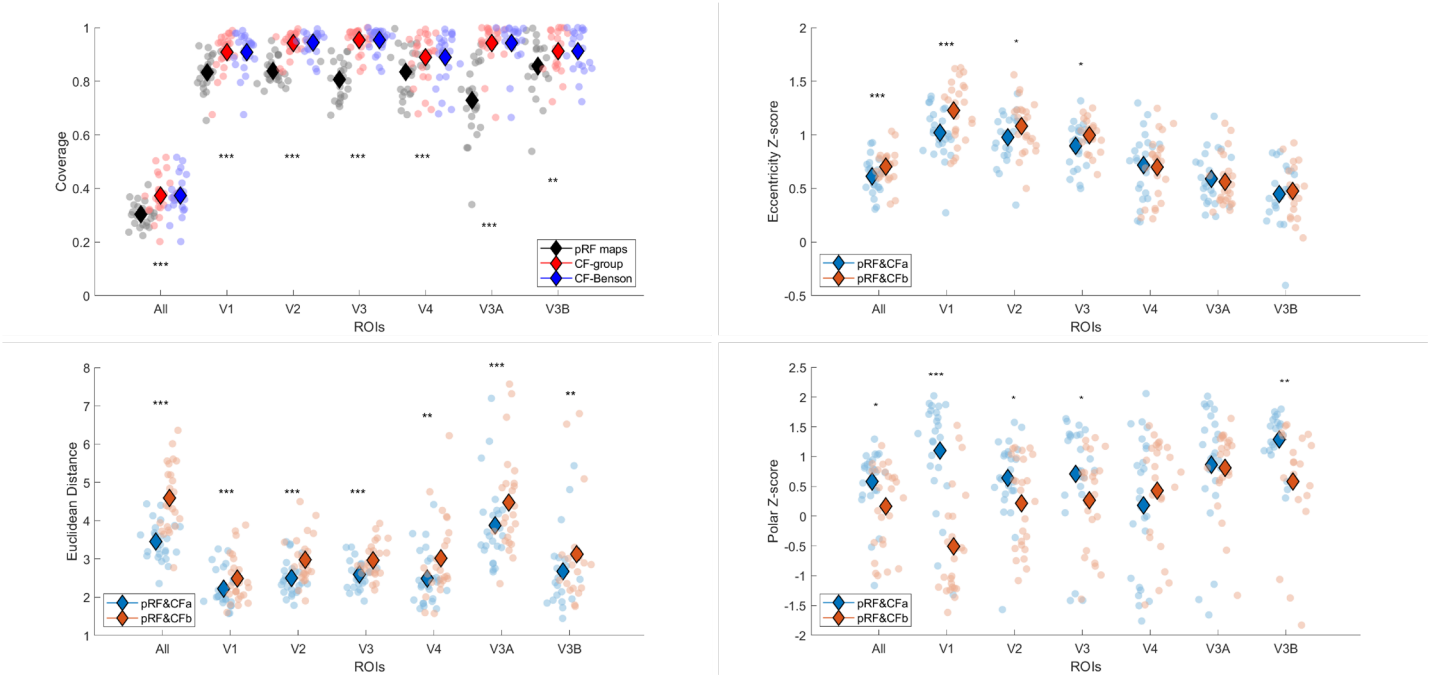


Figure 2: Statistical analyses. Statistical tests were run to assess differences between the analyses for all vertices that passed the threshold of $R^2 > 0.01$ and separately for each visual area, V1-V3B. (A) Friedman's analysis of variance testing the difference between the coverage between the three analyses — pRF, CFa and CFb. (B) The Euclidean 4 distance between the pRFs in the pRF map and the CFa and CFb maps, respectively. Plots comparing the difference between the z-converted eccentricity (C) and polar (D) correlation between the pRF map and the CFa and CFb maps, respectively. *** p<0.001, ** p<0.01, * p<0.05

found that there are differences in map coverage between the two methods, with pRF coverage being significantly lower than the CF. The results here agree very well with the qualitative analysis we conducted.

Next, we compared the CFa and CFb maps to the pRF map; this assumes that the pRF constitutes something of a ground truth for the best possible map that can be obtained for this data. Comparing the correlation between the pRF polar angle estimates (Figure 2D) and those in the two CF maps using a paired t-test showed a significantly stronger correlation for CFa across all vertices and in regions such as V1, V2, V3, and V3B. The results indicate that CFa polar angle maps correlate better with the pRF map than the CFb maps. Despite the CFb template being smoother, CFb polar angle maps lack details and are very crude. This means that on several occasions, polar reversals displayed on CFb are represented by large patches of polar angle reversal with a lack of precise location. Meanwhile, the CFa maps are also cruder than the pRF map, but the locations of polar reversals resemble the conventional pRF map better.

In contrast, we found a significantly stronger correlation between pRF eccentricity (Figure 2C) and the CFb eccentricity in all vertices, and in individual regions such as V1, V2, and V3. This means that the CFb template is more closely correlated to the pRF maps when it comes to the eccentricity mapping. The better correlation found in CFb may be attributed to the template covering the full 90 degrees eccentricity [8], while the CFa template is constrained by the 10 degrees limit of the stimulation screen in the scanner. Since CFa is based on a group average, it contains a statistical artefact manifesting as an eccentricity reversal. As CFb does not pose the same constraints, the eccentricity maps no longer display reversals on the peripheral edge of the visual cortical regions. This therefore becomes more consistent with the conventional pRF eccentricity mapping.

We further investigated the map similarity quantified by the mean Euclidean distance between the position of pRFs and CFs in each map (Figure 2B). Euclidean distances were significantly larger for CFb maps across all vertices and in all individual regions. This indicates that CFb maps captured pRF positions less accurately. That is to say, the CFa maps are overall more similar to the pRF map than the CFb maps.

Future Implications

The current research suggests that the new method of retinotopic mapping can open a window of opportunities. It can help us achieve new ways of testing and research we couldn't have previously done. Conventional visual field mapping studies are prone to several confounds. The prolonged fixation required in the study can pose several problems for studying a wide range of the population. The subject's ability to move their eyes freely is crucial for those with visual disorders such as amblyopia [9] and nystagmus (involuntary repetitive movement of the eyes), and those with other ocular or neurological pathologies. Thus, the new method may provide robustness in the presence of eye movements or a blurred and obstructed visual image [9-10]. Taken together, the method has potential for

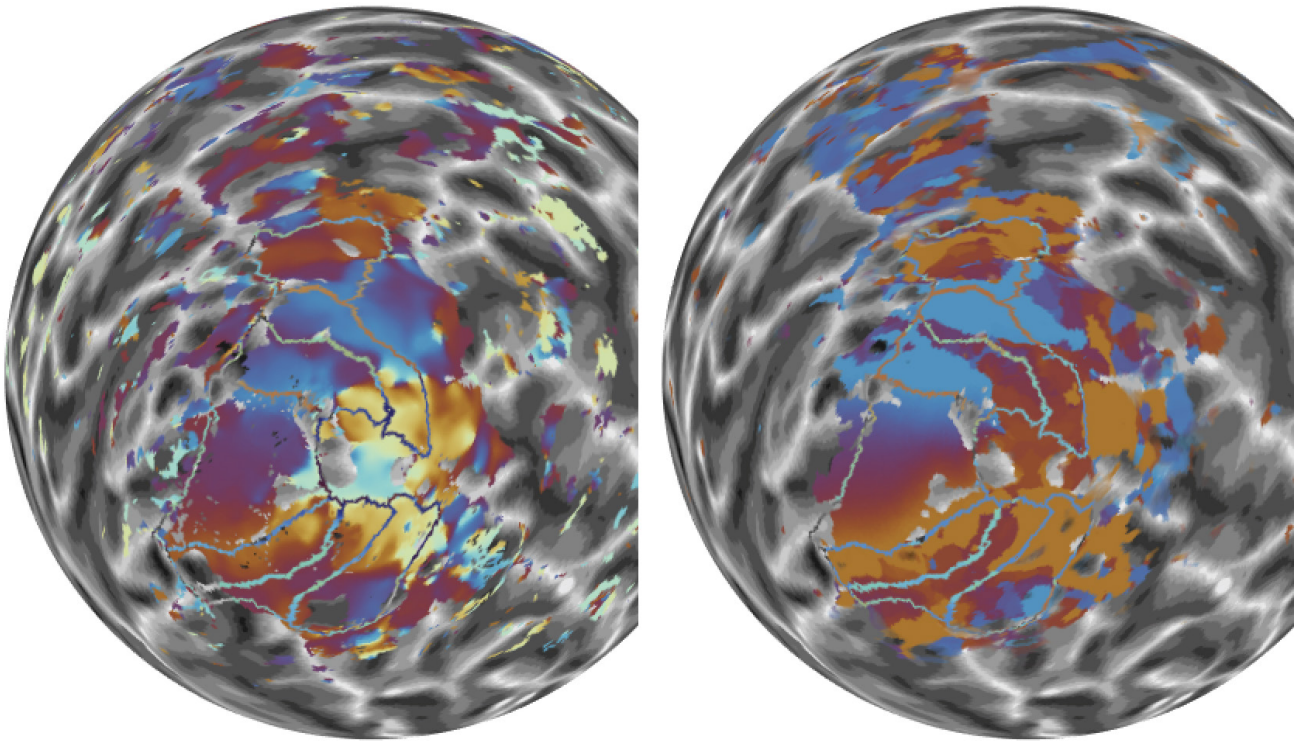


Figure 3: Polar angle maps. Side-by-side comparison between the right hemisphere pRF (right) and the CFb polar angle maps (left).

revealing new insights about visual cortical organisation in various pathologies, as well as in healthy participants at the extremes of the human lifespan.

Another promising implication that this research may lead to is mapping human peripheral vision. Due to several factors, such as the fixation and technological limitations, retinotopic mapping of the human periphery has thus far been considered difficult, or even impossible. The stimulus typically used for conventional retinotopic mapping is often very small, insufficient, and presented near the centre of gaze; therefore, they cannot produce a response in the periphery. The CF method permits movie watching and free eye movements. Thus, it allows the subjects to explore their entire visual field rather than fixating on a single spot [7]. With free eye movements, we can now ensure that the subject's eye movements cover the whole visual field, including the far periphery. Moreover, it enables researchers to use more engaging and interesting stimuli than what was used in conventional pRF mapping experiments, thus helping enhance the participant's motivation, and improve data quality.

Retinotopic mapping with connective field modeling is relatively new, and there are yet to be many studies on the topic. This is the first comprehensive comparison that assesses the quality of retinotopic maps generated by the connective field modeling method. Our results show that there is still substantial room for improvement for this cutting-edge methodology. The results from the current study will help us point towards methodological improvements. We have already begun work on a new approach: while our analysis shown here determined the peak correlation between the position in the visual field and the voxel response to determine the predicted pRF coordinates, our new approach does the opposite. It uses the predicted pRF coordinates from the template to project the correlations into visual space, and then fits a pRF to those correlations in visual space. In addition to estimating pRF position, this approach therefore also estimates pRF size. Moreover, it frees the CF analysis from the constraint that it needs to be conducted separately in each cortical hemisphere. Once we test these improvements, the next step we intend to do is to quantify the hypothetical robustness of this new CF map in the presence of eye movements.

Gene Tang - BAdvSci(Hons), Psychology

Gene is a 3rd-year Psychology student who is currently interested in the field of cognitive and visual neuroscience. During the summer, he did his research project with the School of Optometry and Vision Science with a focus on human retinotopic mapping. He also decided to conduct a year long research project, aiming to use the connective field modelling method to map human peripheral visual field.

Pinpointing Breast Cancer From a Bioengineering Perspective

Max Dang Vu

In 2020, around 2.3 million women globally were diagnosed with breast cancer, the most people for any cancer type. Simultaneously, almost 685,000 women died from the disease [1]. Breast cancer treatment involves locating tumours early and completely removing them through surgery. To enable this, tumour positions are first analysed and identified across medical images acquired from different diagnostic procedures. Based on these analyses and palpations, the surgeon marks the location to perform a tumour excision. But what are the clinical challenges of breast cancer diagnosis & treatment, and how can we help address them from a bioengineering perspective? This article highlights these challenges and reviews state-of-the-art biomechanical approaches to help find solutions to this question.

Clinical breast cancer diagnosis and treatment procedures

Breast cancer diagnosis involves three imaging procedures: X-ray mammography, magnetic resonance imaging (MRI), and second-look ultrasound (Figure 1). A challenge with this is finding the correspondence of tumour positions between the different procedures because breast tissues undergo large displacements with small changes in patient positioning. The patient stands upright during X-ray mammography, with two plates compressing their breasts to achieve near-uniform distribution of internal tissues [2]. However, tumours and normal breast tissue can appear similar on mammograms, increasing the difficulty in differentiating them [3]. MRI is more effective at discriminating lesions from breast tissue due to the high-resolution contrast between soft tissues [4]. Patients lie face-down (prone position) as gravitational forces separate out tissues in the breast [5]. However, while MRI has high sensitivity, it also has low specificity, making it challenging to differentiate lesion types. This can result in unnecessary biopsies to confirm the presence or absence of tumours. Second-look ultrasound can supplement MRI by visualising lesions in real-time and help catch early-stage cancers. Clinicians apply a handheld high-frequency transducer probe over the patient's breast as they lie face-up (supine position) and tilted to one side to obtain these images [3]. Ultrasound, however, has poor cancer detection sensitivity and is best used to supplement MRI [6].

Clinicians typically treat diagnosed tumours by surgically removing them, either through lumpectomy plus radiation or a mastectomy [7]. The intention is to remove tumours altogether to minimise cancer recurrence and optimise survival chances [8]. A lumpectomy eliminates tumours along with small amounts of surrounding healthy tissues to conserve as much of the breast as possible. Follow-up radiation ensures any leftover cancer cells are eliminated or shrink in size for future removal. A mastectomy removes the entire breast when previous treatment strategies are ineffective for patients. This prompts the need for tools that assist in accurate tumour localisation and minimise the removal of healthy breast tissue in treatment.

State-of-the-art development in the literature

These clinical challenges have motivated the development of physics-driven computational models that predict breast biomechanics. The models can simulate motion under gravity loading from the prone position to the supine position, where surgical treatment is performed. This enables

Figure 1: Breast cancer diagnostic images are taken via X-ray mammography in the standing position (a), followed by MRI in the prone (face-down) position (b) and second-look ultrasound in the supine (face-up) position and tilted to one side (c). Image a is obtained from Monkey Business - stock.adobe.com. Image b is from siemens.com/press. Image c is from Luisandres - stock.adobe.com.

radiologists and surgeons to track the features of interest during clinical procedures [9], [10]. Breast biomechanical models are built using the Finite Element Method (FEM), which divides a geometry of interest into a mesh composed of many smaller elements. Partial differential equations describing the breast's mechanical behaviour are solved to predict the breast tissue deformation [11]. Deformation describes an object's changing shape and size in space under applied forces.

Obtaining accurate predictions from biomechanical models requires identifying the mechanical properties of breast tissue. These properties provide insights into breast tissue composition as its underlying architecture and biological environment dictate their mechanical moduli or stiffness [12]. The breast is internally composed of adipose and fibroglandular tissues [13], and their reported stiffnesses vary with different mechanical loading conditions and experimental protocols used for their identification [14]. From the testing of excised samples of tissues (ex-vivo), the general observation is that fibroglandular tissues are 1 to 6.7 times stiffer than adipose tissue [13], and tumours have significantly higher stiffnesses that increase with cancer growth [15]. Researchers typically assess tissue stiffness in-vivo to avoid tissue removal and subsequent damage that may alter their mechanical behaviour during testing [16]. However, identifying mechanical properties in-vivo requires a rich dataset acquired either from MR imaging of the breasts in multiple positions or capturing surface deformation of the breast under indentation using multi-camera systems [10], which is highly challenging to obtain. Therefore, the validation of these identification methods is typically conducted first by performing experiments on soft silicone gel phantoms. These can be moulded into different shapes, such as rectangular beams or the breast [17-18].

At this point, tumours have been identified via imaging, and their locations predicted using biomechanics during surgery. This information is to be communicated to clinicians to assist in tumour localisation. Existing approaches display these predictions on a 2D interface [10]. However, such communication should be more intuitive to improve treatment outcomes. Head-mounted holographic augmented reality (AR) systems have the potential to visualise tumour locations directly on patients during clinical procedures [19-20]. These systems have been successfully trialled in orthopaedics [21] and neurosurgery [22] because the tissues of interest deform minimally during interventions. Perkins (2017) [19] found that aligning holograms to the breast is far more challenging, as the breast significantly deforms with small positional changes. However, proof-of-concept studies combining AR systems with biomechanical models by Gouveia (2021) [20] demonstrated some promise. Clinicians could visualise the identified tumours from diagnostic images on their view of patients before interventions.

Clinical translation challenges of these developments

While proof-of-concept demonstrations have been developed, researchers must address the following challenges to enable routine use of this technology in the clinic. Firstly, state-of-the-art FEM simulations can take 30 seconds or longer to run [23], which is slower than the 60 frames-per-second required to reduce nausea and disorientation [24]. A proposed solution is surrogate models, which uses machine learning to accelerate the evaluation of the models but maintain similar accuracy to FEM models. Studies using decision trees, randomised trees, and random forest models have enabled breast tissue deformation predictions under compression in about 0.15 seconds [25]. However, these approaches require training surrogate models offline for each patient that will be considered, which can be time-consuming. Studies in the breast biomechanics literature have utilised trained models from a previous problem to predict the mechanical behaviour of a new dataset [26]. Secondly, estimating mechanical properties is also a computationally intensive procedure, often taking hours to complete. The model parameters that describe, for example, the stiffness of breast tissues are tuned iteratively to best match measured breast shape under known loading conditions [14]. Clinical use requires this process to be much faster. Thirdly, clinicians need their AR headset to align the 3D hologram dynamically with the object of interest as they move their heads around. Studies in the literature have assumed the breast is rigid, making it difficult to align the model hologram with the real breast [19-20]. The breast must align with a deformable model that incorporates mechanical properties to account for how even small changes in patient positioning can alter breast shape.

Objectives of the PhD

The challenges above have motivated me to develop an integrated physics-driven AR software platform that will provide navigational guidance to clinicians for tumour localisation. My platform will extend an automated clinical image analysis workflow developed by the Breast Biomechanics Research Group at the Auckland Bioengineering Institute [10] to align diagnostic images directly onto a clinician's view of a patient during breast cancer treatment procedure (Figure 2).

One of my platform's key features is near real-time simulation of breast tissue motion using surrogate models that incorporate information from population-based breast shape analyses. This will enable the surrogate models to provide predictions without time-consuming offline training. I will also integrate surrogate models developed in-house [27] with skin surface measurements from sensors

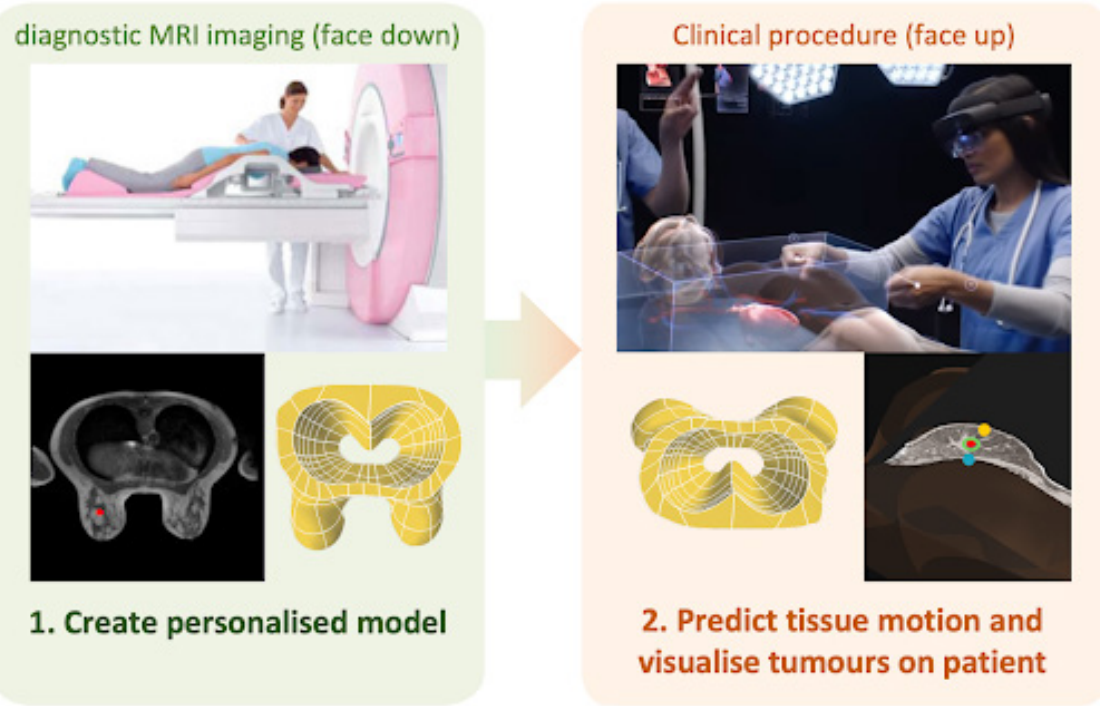


Figure 2: My proposed physics-driven AR platform will leverage an automated clinical workflow for breast cancer image analysis [10]. The workflow builds personalised biomechanical models of the breast from diagnostic MRI and visualises breast tissue displacements in near real-time during clinical procedures performed in supine. In addition to technical developments for accelerating the workflow and identifying mechanical properties of the breast, my work will replace the GUI with an AR workflow that aligns diagnostic images to the clinician's view of patients. Images are obtained from Romaset - stock.adobe.com

on AR headsets (Figure 3) to enable estimation of breast tissue stiffness under known loading conditions (changes in an individual's posture which changes the gravity loading conditions the breast experiences). The platform will integrate these developments with fiducial markers placed on the breast surface, and shape measurements from AR headset sensors to enable dynamic alignment of biomechanics simulations to the patient. The platform will apply the tissue displacements predicted by the mechanics simulations to the diagnostic prone MRI to help clinicians visualise how the internal tissues change shape in the supine position. This will help clinicians co-locate regions of interest across modalities e.g. between MRI and second-look ultrasound images. I will develop the platform in my first year and incorporate it into a state-of-the-art AR headset (Microsoft HoloLens 2 shown in Figure 3). The platform's accuracy for predicting supine tumour locations will be validated during platform development on soft silicone gel

Figure 3: A diagram of the Microsoft Hololens 2 AR headset to be embedded with the developed software platform. Clinicians will be wearing these during procedures to visualise the predicted tumour locations onto patients directly. This image is from the Microsoft News Center Image Gallery.

phantoms with tumour-like inclusions. In subsequent years, I will evaluate the platform's performance on patients in a series of clinical pilot studies.

Breast cancer research is fast becoming an interdisciplinary field. Whether it is medical image registration, large deformation mechanics modelling, or computer vision, research opportunities are growing to address the field's significant challenges. I hope my work contributes to increasing the accuracy and efficiency of breast cancer treatment, improving health outcomes, and saving more lives.

Acknowledgements

External editors

I want to thank Dr Prasad Babarenda Gamage and Dr Gonzalo Maso Talou for their guidance throughout the editing process, for approving the article proposal, and for supervising my PhD study in the ABI's Breast Biomechanics Research Group.

Funding

The ABI's Breast Biomechanics Research Group is grateful for the funding we have received from the University of Auckland Foundation, the New Zealand Breast Cancer Foundation, and the New Zealand Ministry of Business, Innovation and Employment that has supported our research. I would also like to thank The University of Auckland for awarding me a Doctoral Scholarship to support my PhD study financially.

Max Dang Vu - PhD, Biomedical Engineering

Max recently graduated from UoA with a BE(Hons) in Biomedical Engineering. His PhD work at the Auckland Bioengineering Institute investigates how physics-driven soft tissue models and augmented reality techniques can enable navigational guidance during breast cancer diagnosis and treatment procedures.

Einstein's Miracles, Part 2: Atoms

Caleb Todd

Atoms are a deeply familiar part of our natural world. Their name is taken from the Greek *atomos* (meaning 'indivisible', despite the fact that atoms have constituent pieces into which they can be divided) because they constitute the fundamental unit of a chemical element. If you take a helium atom and try to break it up — divide it — what you have left is no longer helium.

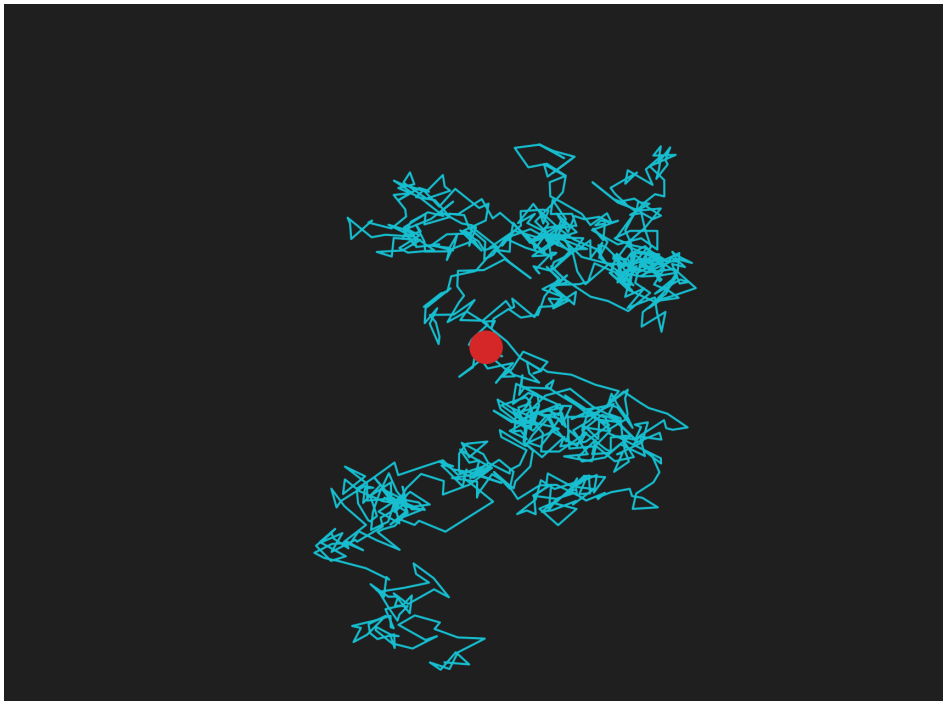


Figure 1: A simulation of a particle undergoing Brownian motion. The red particle jittered randomly along the blue curve.

We are quite comfortable, these days, with the idea that atoms are matter's building blocks, but universal acceptance thereof is actually a relatively recent development. While the idea of atoms goes back to ancient Greece, where scholars like Leucippus and Democritus proposed indivisible units of substance, these were philosophical arguments, not scientific [1]. Those who were more rigorous had to wait until around 1800 AD before atomic theory really developed as a science [1], and when our frizzy-haired protagonist came along in the early 20th century, there was still debate over its validity.

In our last issue[1], we began the story of Einstein's *annus mirabilis* papers by highlighting his work on the quantum nature of light. He helped launch the quantum revolution which subsequently redefined and recontextualised all of physics. The significance of that paper was only recognised slowly, though, so Einstein decided that if one revolutionary paper per year wasn't enough, he'd just have to write two[2]. As such, he turned his mind to the matter of matter and published *'Über die von der molekularkinetischen Theorie der Wärme geforderte Bewegung von in ruhenden Flüssigkeiten suspendierten Teilchen'* ('On the movement of small particles suspended in a stationary liquid demanded by the molecular-kinetic theory of heat') in Annalen der Physik, 18 July 1905 [2].

At the heart of Einstein's discussion lies the phenomenon of Brownian motion[3]. If you suspend a very light particle (like a mote of dust, for example) in a fluid and place it under a microscope, you will see it randomly zigzag and jitter [3], like in Fig. 1. Though no objects are visibly colliding with it or exerting a force on it, the particle is still continuously changing its motion. Is this a violation of Newton's first law of motion? Certainly not. Instead, we might suspect that there are invisible objects colliding with the particle causing its variation in speed and position — and if they are invisible, they must be very small indeed. Perhaps Brownian motion is caused by atoms, which were proposed by the chemist John Dalton to explain how some substances can combine to make other substances. This is the explanation that Einstein proposed, but proposals and proofs are two very different beasts.

At the same time, there was another thread in physics running parallel to the question of atoms: what is heat? What property of a substance makes it hot or cold? For a long time, scientists thought that there was an invisible fluid that imbued heat to the objects around which it flowed[4]. That notion was dismissed, however, when James Joule demonstrated that heat was just another form of energy[5] [4] — but what kind of energy? This is where the 'molecular-kinetic theory of heat' in Einstein's title comes in. In this theory, heat energy is really kinetic energy; that is, the energy

[1] Available on our website.
[2] I might be projecting motivations a little bit here.
[3] Thankfully this has nothing to do with digestion. It is named after its discoverer Robert Brown
[4] Physicists often invent imaginary fluids to grapple with phenomena they don't understand, as we will see in the next part of this series when we discuss the aether and light speed.
[5] Essentially all engines and electricity generators depend on this principle. The SI unit of energy is named the Joule in his honour.

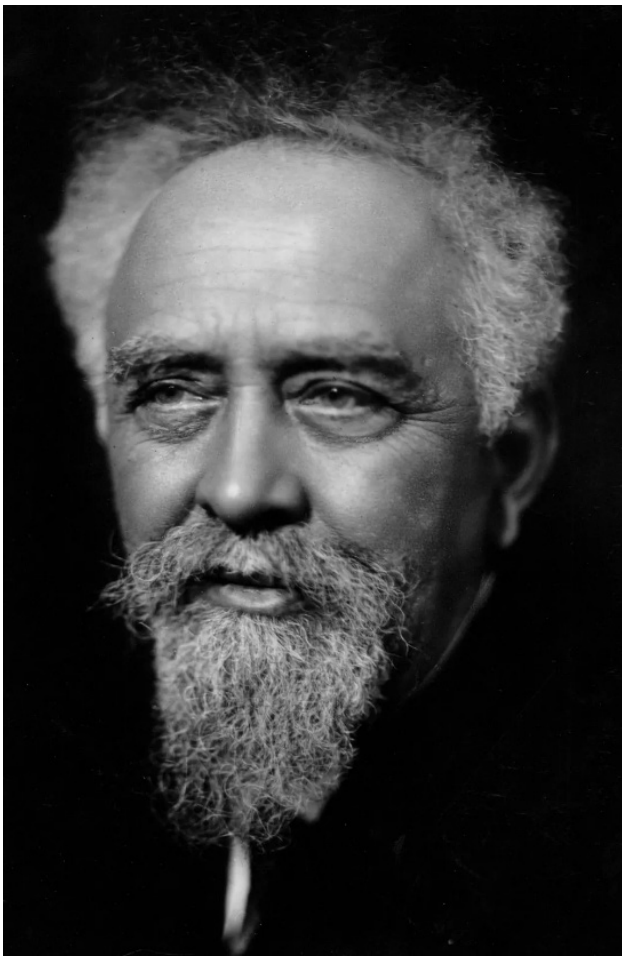


Figure 2: Jean Baptiste Perrin, French physicist and winner of the 1926 Nobel Prize for demonstrating the existence of atoms. Image taken from Encyclopædia Britannica.

associated with motion. In particular, it purports that heat is the kinetic energy of the atoms (or molecules) that make up a substance. You can now, perhaps, see how these threads tie together. If atoms exist and the kinetic theory of heat is correct, Brownian motion can be directly explained as collisions between the jittering particle and hot atoms in motion[6].

It seems a very cogent theory, but that in and of itself does not place these questions beyond doubt. We need something measurable that could experimentally validate Einstein's conclusions. For this reason, one of the most significant parts of his paper is a mathematical expression for how quickly particles undergoing Brownian motion spread out from their initial positions. As it turns out, this average speed depends on the fundamental properties of the atoms being theorised about. So, by measuring Brownian motion, a physicist could help substantiate (or discredit) the kinetic theory of heat.

Einstein did not have available to him sufficient data to actually draw a conclusion. Rather than trying to do the experiment himself, he simply concluded his paper by saying (in German), "Let us hope that a researcher will soon succeed in solving the problem posed here, which is of such importance in the theory of heat!" [2]. Fortunately for Einstein (and all other theoretical physicists), there are plenty of experimentalists who are willing to actually check whether the nonsense they write down is true. In this case, it was a Frenchman by the name of Jean Baptiste Perrin, whose experiments concluded (lo and behold) that Einstein's predictions were correct[7] [5].Atoms do exist, the molecular-kinetic theory of heat works, and we've never looked back since.

Though it would be disingenuous to suggest that this result was totally surprising to the physics community — atoms and kinetic heat were well-regarded theories — it was absolutely still a controversial topic when Einstein's paper was submitted. The importance of atomic theory need hardly be restated, and Jean Baptiste Perrin was awarded a Nobel Prize for his experimental verification of Einstein's theory [5]. Note that this is the second of Einstein's 1905 papers connected to a Nobel prize (although not for Albert himself, this time). Einstein is two-for-two[8]. This paper on Brownian motion is often overlooked in the *annus mirabilis* because of how revolutionary quantum theory and special relativity (the subjects of the other three 1905 papers) are, but that is somewhat unfair to an incredibly significant paper. We are now living in the 'Atomic Age', but barely a century ago we weren't even sure that atoms existed.

For the second time in just two months, Albert Einstein had changed the way we saw the world — but he wasn't finished yet. In the next edition of the UoA *Scientific*, we will watch Einstein quite literally challenge the structure of reality itself.

Caleb Todd - BSc (Hons), Physics

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[6] The hotter the atoms, the more jittering they cause. Much like in night clubs (or so I am told).
[7] You're shocked, I'm sure.
[8] Although the prizes themselves were, of course, awarded far later than 1905.

The Algol Paradox: How Do Stars Age?

Aimee Lew

Algol is perhaps one of the most storied stars in Earth's night sky.

Going by Beta Persei or the Demon Star (from Arabic: ra's al-ghūl, just like the DC villain), for thousands of years, Algol was considered an omen of death and destruction [1]. The reason for this may have been its variability, or the periodic fluctuation of its brightness. In astronomy, the apparent magnitude is a measure of a star's brightness to earthbound observers. Algol's apparent magnitude dips approximately every three days, which — if perhaps one squints and drinks — could look like the slowly blinking eye of a harbinger of death.

With the advent of telescopy and spectroscopy, astronomers learned in the 1880s that Algol was not one star, but multiple [2, 3]. It comprises three bodies that blur into a bright dot before us. Two of Algol's components, β Persei A and B, orbit and eclipse each other. The passage of one body in front of the other, with respect to the line to Earth, decreases the apparent magnitude.

With more technological breakthroughs in the twentieth century, , the catalogue of star masses, distances from Earth, temperatures, compositions and age grew and grew. Astrophysicists attempted to put together a description for the evolution of stellar bodies. The theory went — and still goes, with more nuanced addendums — that more massive stars age quicker. But the Algol binary was an anomaly: the smaller body had advanced, and the larger body remained in an earlier stage of stellar evolution. Thus, the Algol Paradox was born [4].

Figure 1: The Algol system on 12 August 2009. Image from the CHARA (Center for High Angular Resolution Astronomy) array in California.

To understand why β Persei A and B supposedly defied the trends of stellar evolution, we first need to understand stellar evolution. Think of a star like a furnace. From nebulae, they are born with a certain amount of 'fuel' (hydrogen) in their cores. The amount of fuel a star gets is determined by its mass. In their cores, nuclear reactions are taking place at extraordinary rates and scales. The light of a star comes from the energy output of converting protons into helium nuclei. More massive stars burn fuel at larger rates and scales, so they are hotter, brighter, and deplete their hydrogen sources more quickly [5].

While a star remains in the fuel-burning early stage of their lifetime, they sit on the main sequence. The main sequence is a diagonal band of stars on the Hertzsprung-Russell (HR) diagram [5].

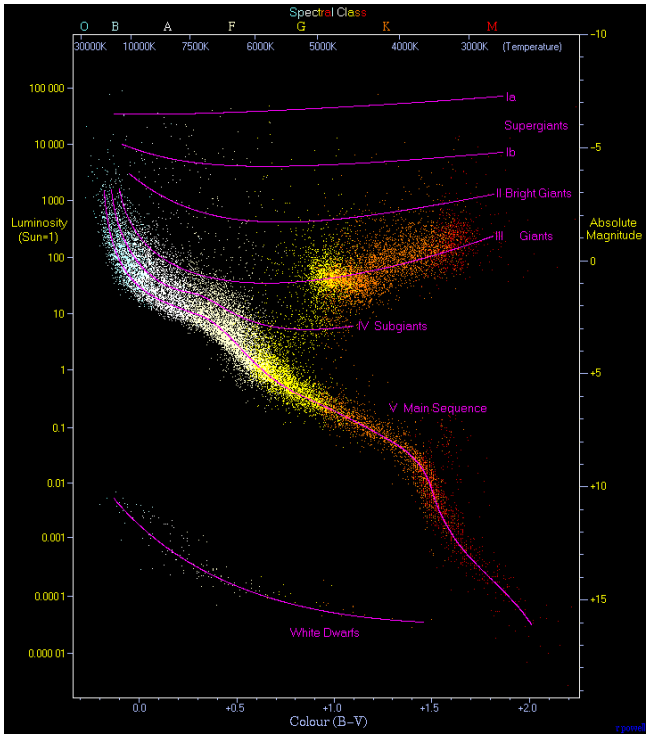

Figure 2: The Hertzsprung-Russell diagram with data from the Hipparcos and Gliese catalogues. HR diagrams compare the luminosities, or brightness, of a star to its stellar colour, or effective temperature. In the upper-left are the hot and bright stars, which appear as white-blue, and in the lower-right are the (relatively) cool and dim stars, which appear as orange-red. Underneath the main sequence are the white dwarves—extremely dense stars that are in their final evolutionary state—and above are the red giants and supergiants.

Astronomers used to think that the main sequence showed the pathway of stellar evolution. Stars would begin their lives in the upper-left, hot and bright, and cool over time, falling into the lower-right corner [5]. But the main sequence of the HR diagram is no more an evolutionary pathway than the band of the Milky Way; both are simply smatterings of stars at some given point in time. All stars are born on the main sequence, their position dictated by brightness and temperature, which is in turn dictated by mass. For as long as nuclear fusion persists in their cores, which is about 90% of their lifetime, they don't move significantly along the diagonal [6]. Larger stars inhabit the upper-left and leave the main sequence fast (cosmically speaking) after a few million years. Smaller stars inhabit the lower-right and can burn for billions of years, like our Sun.

When stars deplete their sources of hydrogen, they evolve. Lower mass stars expand into red giants (large, less dense and cool), then shrink into white dwarves (small, dense and

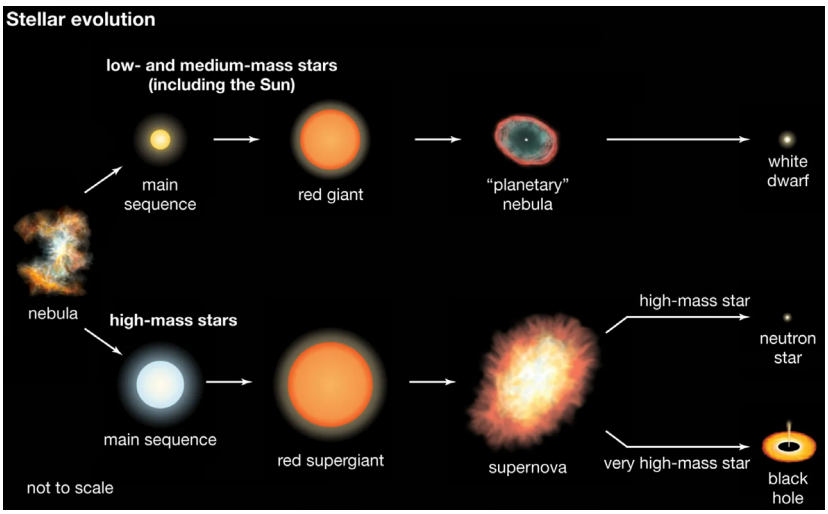

Figure 3: Stellar evolution diagram. Image from Encyclopaedia Britannica, 2012.

hot) which will eventually radiate away all of its energy and wink out. Higher mass stars expand into red supergiants (very large and very cool) that will expand until the outward radiation pressure drops lower than the inward force of gravity. At that moment, red supergiants will crumple and supernova, creating atomic nuclei anew.

In the Algol system, astrophysicists expected the two orbiting bodies to evolve as two individuals, but the observations seemed to suggest the opposite was true [7]. There is a smaller star in the giant phase and a larger star still on the main sequence. To understand the contradiction of Algol A and B's behaviour, we need to focus on two things: red giants and gravity.

Notice that whether a star begins with more mass or less, both classifications have a period of expansion into either a subgiant, giant or supergiant star, which is a later but not final stage of stellar evolution. In binary star systems, the Roche lobe helps to shed light on the Algol Paradox. The Roche lobe defines the region around each star in which matter is gravitationally bound to that star. Roughly teardrop-shaped, the intersection of each lobe is called the Lagrange point. In Algol-type binaries, it's possible for expanding red giants to fill their Roche lobe [8]. When that happens, matter can be transferred away from the initial stellar body. Roche lobe overflow (RLOF) is the culprit for this anomalous behaviour [9].

Astrophysicists now know that binary star systems like Algol A (a hot blue-white main sequence star) and B (a cooler orange subgiant) begin as two close-range stars of the same age and composition—having formed from the same nebula—with different masses. The larger star ceases nuclear fusion and starts expanding into a red giant earlier than the smaller star, as suggested by conventional stellar evolution. At this point, orbiting material that fills the larger star's Roche lobe and surpasses the Lagrange point falls into the gravitational well of the smaller star [10]. As stellar expansion continues, more mass transfers to the smaller body until there appears to be a less massive star (Algol B at roughly 0.7 solar masses) that has burned through all its hydrogen and a more massive star (Algol A at roughly 3.2 solar masses) that is still trucking along [11].

Solved in the twentieth century, the Algol Paradox helped to shed light on the behaviour and evolution of binary star systems. Algol-type binaries remain a hotbed of academic interest, classified as cases "where the less massive donor fills its Roche lobe, the more massive gainer does not fill its Roche lobe and is still on the main sequence and the donor is the cooler, fainter and larger star" [9]. Meanwhile, training a closer and closer eye on Algol revealed in 2020 that the system might contain more bodies than anyone, thousands of years ago, staring up at the blinking Demon Star, could have thought [12]. The history of Algol unfolds alongside the discipline of astronomy and astrophysics, marking with pinpricks of light what we thought we knew, what we do know, and what we have yet to discover.

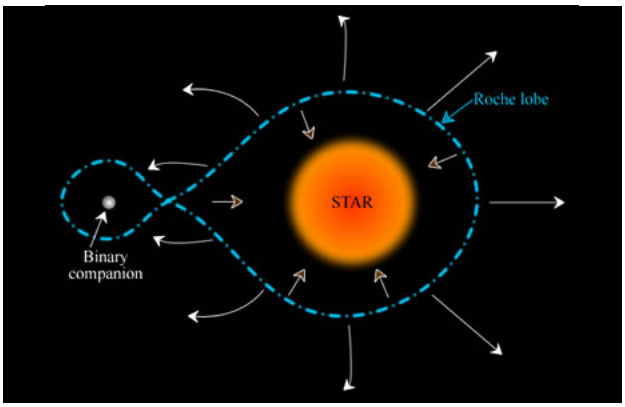

Figure 4: Roche lobes of a binary star system. Image from COSMOS, the SAO Encyclopaedia of Astronomy, Swinburne University.

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Are AIs Smarter than a 5th Grader?

A review of recent developments toward solving the Math Word Problem

Anne Newmarch

The Math Word Problem is a natural language processing (NLP) challenge that has seen exciting progress within the last few years. It requires a machine learning model to read a contextualised math problem, identify the relevant information, and produce an answer for which humans would require multi-step reasoning [1]. Most machine learning models have been trained on primary school mathematics problems to scale to higher levels of complexity after high accuracy is achieved.

This article will discuss some recent academic papers addressing the Math Word Problem. While it is easy to conclude that a paper is better based on accuracy rates, it is important to note that such accuracy rates may be contingent on the dataset for which the model was trained. If an independent test of questions that were created for a primary school level were given to these models, it is unclear which would outperform the others. Ultimately, it may depend more on the questions' nature than the models themselves.

One approach to solving the Math Word Problem is to generate an expression tree from which computing the final answer is rudimentary. Reading the tree from the bottom up reveals the multi-step reasoning needed to solve the problem.

A paper from Singapore Management University in 2020 [1] generated this type of solution with their novel Graph2Tree model. Their fully supervised approach processed the input and extrapolated the quantities and related words. This information was then projected onto a graph. This graph

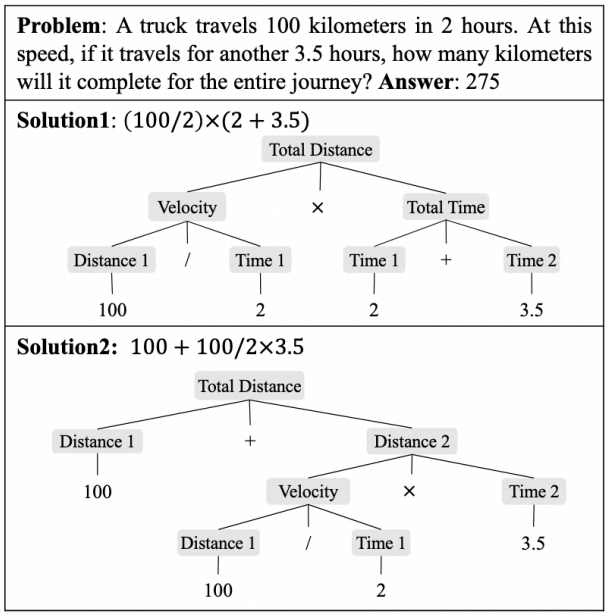


Figure 1: Exemplar MWP with multiple solutions.

An example of two expression trees which both evaluate to a correct answer for a Math Word Problem. Hong et al. [4]

displays the relative relationships between the concepts of the question. A graph convolution network (GCN) and a tree-based decoder were then used to produce an expression tree. The model was tested against questions from the MAWPS [2] and Math23K [3] datasets, resulting in one of the highest accuracy scores for this problem at 77.4% on Math23K.

A more recent approach by Hong et al. last year [4] also generates a solution tree, but instead uses weakly-supervised learning. Fully supervised learning uses the correct answer and solution tree as the target of the learning algorithm. They argue that this restricts the variety of solutions as only one way of reaching the correct answer is produced. There are many distinct approaches to solving these problems, so the study did not train to the tree — only the correct answer. This ultimately allowed the model to suggest a range of correct ways to arrive at the same solution. Furthermore, Hong et al. took an interesting new approach by programming the model to fix its own mistakes by trying out different values in the incorrect expression tree to find the correct answer. This was to more closely imitate the way humans learn, coined by the researchers as 'Learning by fixing' [4]. If a correct solution was reached, it was then committed to memory to encourage more diverse solutions. The researchers proved that their model generated a range of different solutions to the same problem at 45-60% accuracy on Math23K.

A different approach to solving the Math Word Problem is to use a verifier to improve accuracy, as demonstrated by a paper from OpenAI headed by Cobbe [5]. The researchers proved that a verifier given a range of proposed generated solutions could accurately evaluate the probability that a proposed solution was correct. The solution with the greatest probability of being correct was chosen for output. Cobbe et al. proved that this approach ultimately increased the accuracy of a fine-tuned model by as much as 20%.

However, all this research appears to have been shot out of the water by a recent paper released this year in a joint effort from MIT, Columbia University, Harvard University, and the University of Waterloo [6]. Drori et al., in their self-professed 'milestone' [6] paper, have produced a transformer model capable of solving math word problems at a university level with perfect accuracy. The model can also produce these university-level problems well enough that students cannot correctly identify whether the problem was machine-generated 100% of the time. As this model requires no additional programming between switching course content, the researchers state that it could be applied to any STEM course.

There is, however, a caveat to this, and it is not a small one: Drori et al. essentially solved a slightly different problem than previously discussed, as their model requires additional

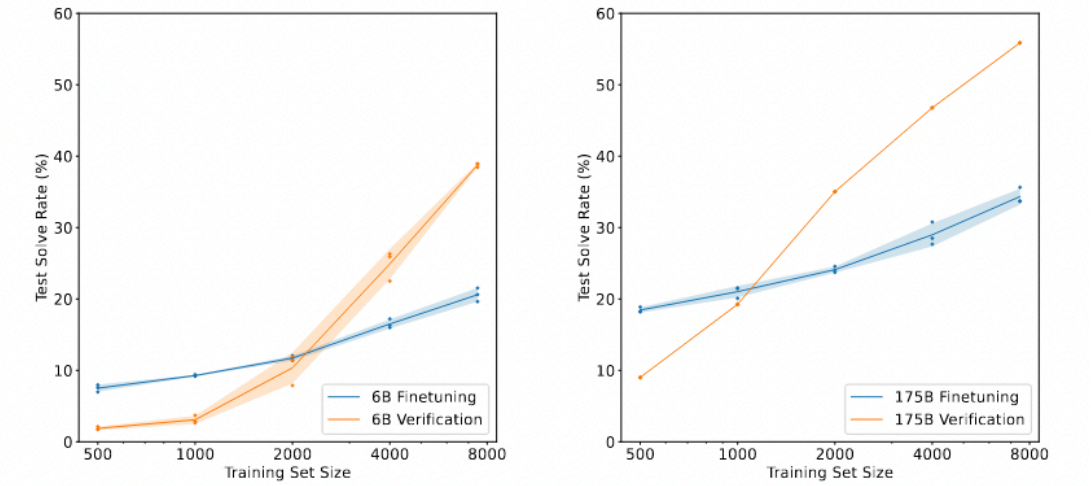


Figure 5: A comparison between finetuning and verification using 6B and 175B model sizes. Verification considers 100 solutions per problem. Mean and standard deviation is shown across 3 runs, except for 175B verification which shows only a single run.

A comparison between finetuning and verification on 6B and 175B models. Given a large enough training set, the test solve rate of the verification model will surpass that of the finetuned one. Cobbe et al., [5]

contextual information with the input text. They attribute their success and previous research failures to this fact.
The model [6] works as follows: an input question is tidied and given additional contexts, such as the mathematics topic, and the relevant programming language and libraries. The researchers report that the majority of the questions required minor or no modifications. A portion of the modifications could be done automatically, while the rest is inferred to have been done manually. The transformed question is then fed to the OpenAI Codex Transformer [7], a highly successful machine learning model that takes in text input and generates corresponding code. The produced program is then run to achieve the correct answer.

The researchers argue that providing this additional key context is fair, as the students who take these courses rely on implicit knowledge for their answers. Additionally, further research may improve this model to fully automate question modification.

This recent development has not been without backlash. In a paper published only 20 days after Drori et al., Biderman and Raff [8] take the stance that this type of machine learning research 'has not engaged with the issues and implications of real-world application of their results [8]. They argue that machine learning models like that of Drori et al. will be abused by students cheating, especially given that results are often not flagged by plagiarism detection tools.

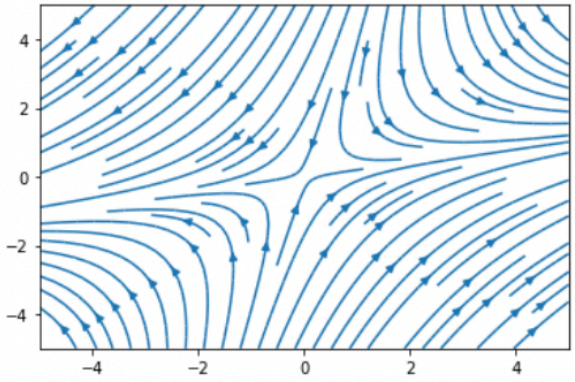
They are correct that students will use these models to cheat if given mainstream access. However, this is not a new situation: a primary school student cheating on their times-tables homework with a calculator is not so functionally different from a university student cheating on their calculus assignment with this model [6]. The result is the same: neither student is likely to perform well under test conditions. For online exams, a tool such as this disappears into the haze of students' many methods to cheat.

While Drori et al. [6] have found success, this is not the end of the road for the previous research. The Math Word Problem is not only about solving the questions themselves – it is about learning how we can improve on our machine learning techniques to facilitate reasoning. If we believe that there are problems we want to solve that require reasoning that cannot be programmed, then developing research into graphical representations of relationships and learning by fixing could be crucial to success. All progress and the effort researchers put into these methods are valuable.

Table 70. MIT 18.03, Question 18: Original question, Codex input and output, and solution.

Topic	Stability and the Phase Plane
Original question	Find the critical point or points of the given autonomous system, and thereby match each system with its phase portrait. $dx/dt = 2 * x - y, dy/dt = x - 3y$
Codex input	dx/dt=2*x-y, dy/dt=x-3y Use Sympy to print the critical points. Afterwards, plot dx/dt=2*x-y, dy/dt=x-3y using streamplot

Codex output	`import sympy as sp`
	`import matplotlib.pyplot as plt`
	`import numpy as np`
	
	`x, y = sp.symbols('x y')`
	
	`f1 = 2*x - y`
	`f2 = x - 3*y`
	
	`critical_points = sp.solve([f1, f2], [x, y])`
	`print(critical_points)`
	
	`x_range = np.linspace(-5, 5, 100)`
	`y_range = np.linspace(-5, 5, 100)`
	
	`x_mesh, y_mesh = np.meshgrid(x_range, y_range)`
	
	`dx = 2*x_mesh - y_mesh`
	`dy = x_mesh - 3*y_mesh`
	
	`plt.streamplot(x_mesh, y_mesh, dx, dy)`

Solution	$\{x : 0, y : 0\}$ 

Each step of the transformer model, from original question to its modified version, the program generated by Codex, and the output given as an answer. Drori et al. [6]

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The Ecology of Undesirable Organisms

Jasmine Gunton

Vita (English: 'Life')

An integral part of human nature is to place every object in the universe into a hierarchical ranking system. We can see these hierarchies in social constructs such as class distinctions, businesses, and political systems. Additionally, hierarchies have an established role in science, with many biologists over human history attempting to place the Earth's many living organisms into a structured grouping. The most common of these ranking systems today is the Linnaean taxonomy. In this system, different species are grouped into a kingdom, phylum, clan, and so on [1]. However, other systems are still insidiously ingrained into the human understanding of biological theory, with one of the prime examples being the 'tree of life'. The tree of life places humans at the top of the proverbial tree, supposedly being the most intelligent and sophisticated animal. 'Inferior' species such as apes and reptiles are placed at lower branches. Finally, the prokaryotes are placed at the base of the trunk, being deemed as the most simple and unintelligent creatures [2].

The discipline of ecology challenges this old view, instead opting to view organisms in the context of the highly complex ecosystems in which they occupy. Ecology recognises that each species within an ecosystem contributes greatly to the functioning of that ecosystem through indirect and direct interactions with other organisms and their environment. Nevertheless, some organisms are still viewed by the public as ecologically useless and undeserving of conservation efforts. I would like to explore why such creatures are, in fact, biologically important, and why their identity in popular culture should be reconsidered.

Rattus

Rats are one of the first creatures to come to mind as being universally disliked. This reputation has been sculpted by the rodents' tendency to spread deadly pathogens and parasites to humans [3]. But you already know why rats are considered repugnant. Instead, let us look at why this rodent is beneficial to its native environments. Along with various pathogens, rats are also transporters of mass quantities of plant seeds. For example, in southwest China, Edward's long-tailed rat (*Leopoldamys edwardsi*) is the main dispersal vector of the seeds of the tea oil camellia (*Camellia oleifera*). It just so happens that the long-tailed rat is also a voracious consumer of these seeds. In true rodent fashion, the long-tailed rat will hoard the seeds it has collected in various subsurface burrows. This effectively disperses the tea oil seeds, increasing the population's chance of survival. The survival of tea oil camellia is therefore directly dependent on the abundance of long-tailed rats within the region [4].

Another important rat species is the Californian giant kangaroo rat (*Dipodomys ingens*). In the sandy grasslands of California, the kangaroo rat acts as a keystone species and habitat engineer of the ecosystem. Services provided by the kangaroo rat include soil disturbance and the creation of vast burrow networks that act as a habitat for other native species. By changing habitat structure, the kangaroo rat alters the community composition of the ecosystem, exerting positive effects on plant and invertebrate diversity, as well as lizard and squirrel abundance [5]. The vital presence of rats in these community structures conveys their ecological importance. It is important to note that in these situations, rats are native to the community, unlike in New Zealand where they are considered a threat to native ecosystem structures.

Fungi

It is not only animal species that receive negative attention from the human population. Mould, as many websites would tell you, is undesirable to have in the home as it releases mycotoxins that can be harmful to humans [6]. While not particularly useful within a house, mould has many benefits for its native ecosystem. Now, just to make things clear before explaining its ecology, mould is neither an animal nor a plant. It is instead part of the eukaryotic group of organisms known as fungi. This means that mould and other fungi species are *special*, and *not like the other organisms*. The taxa 'mould' has been given to multiple polyphyletic groups of fungi, so for the sake of simplicity, we will treat both fungi and mould as if they are the same. Native to every continent, fungi are incredibly hardy and ancient, having evolved symbiotic relationships with several plant and animal species [7-9]. One of the most important roles that fungi play is the decomposition of organic material. In almost every ecosystem, the same cycle of decomposition takes place.

When organisms die, their bodily material is digested by various species of fungi. This digestion process converts the organic material into nutrients that plants can use. Herbivorous animals eat these plants, the animals eventually die, and the cycle is renewed. Fungi can also benefit plants through a mutualistic relationship known as mycorrhizae. Mycorrhiza is a symbiotic association between a fungus and the roots (or the rhizosphere) of a plant. The plant supplies sugars from photosynthesis to the fungi, and the fungi in return supply the plant with water and nutrients such as phosphorus and nitrogen, which are taken from the soil [10]. For some plant species, mycorrhizae are essential for the effective establishment and growth of the plant. Therefore, the survival of certain plants in an ecosystem depends on the existence of, and services provided, by fungi [11].

Vespidae

Ample information has been included in this article concerning the benefits provided by foragers and decomposers. Now I want to discuss the question, how do predators benefit their respective ecosystems? One cannot deny that wasps are menacing, aggressive, and persistent in their violence. Yet, these qualities are what make wasps such beneficial predators in their ecosystem. Once again, this discussion of the benefit of wasps to their environment is focusing on their native environments. Wasps prey on a number of insects, including caterpillars, cicadas, flies, and beetles. By feeding on these carnivorous and herbivorous insects, the wasp indirectly protects both insects and plants in the lower levels of the food chain [12]. However, wasps are only predators of insects in a certain sense. Adult wasps do not actually eat insects, preferring instead to paralyse their prey and feed it to their larvae [13]. Nevertheless, this process ensures that certain insect species do not become over-abundant in the ecosystem. As well as performing natural regulatory services, wasps have substantial potential to act as biological pest control agents in urban and pastoral regions. A study by Prezoto et al. suggests that wasp colony management is a cost-effective and feasible technique in controlling pest species [14]. It is not only their violent nature that makes wasps an asset to their ecosystem. In addition to predation, wasps also act as pollinators for a large range of plant species (which is a fact I'm sure bee enthusiasts greatly detest). In fact, Brock et al. found that 164 plant species were solely dependent on aculeate wasps for pollination [12]. Perhaps we should display the same amount of appreciation for wasps as we do for another certain flying insect.

Columbidae

The last example I wish to discuss has been described by some as a 'flying rat'. This species often inhabits cities and feeds on food scraps discarded by humans [15]. I am talking about none other than the pigeon. Despite once being used by humans for communication, pigeons have sadly earned a reputation less than favourable [16]. It is thus my duty to convince you, the reader, of the pigeon's usefulness in its ecosystem, and to inform you of its charismatic qualities. Similar to the long-tailed rat, pigeons are important distributors of plant seeds. Pigeons are especially effective at seed dispersal as they travel long distances away from the parent plants. For example, the New Zealand Kererū (*Hemiphaga novaeseelandiae*), or 'wood pigeon' is an important seed disperser of the native tree species *Beilschmiedia tawa* (Tawa), *Vitex lucens* (Pūriri) and *Pseudopanax arboreus* (Five-finger) [17]. In other countries, pigeons are an important food source for many species of falcons, including the peregrine falcon (*Falco peregrinus*) [18]. The peregrine falcon itself is also important in its ecosystem as a predator of several other bird species, including ptarmigan and ducks. Therefore, by supporting peregrine falcon populations, the pigeon indirectly helps to regulate other bird species [19]. Another interesting fact (that admittedly does not have much to do with its ecology) is that pigeons have excellent visual discrimination skills. A study by Watanabe et al. showed that pigeons can be taught to discriminate between the artworks of Claude Monet and Pablo Picasso [20]. In a later paper, Watanabe displayed that it was possible to teach pigeons how to discriminate between the paintings of other artists, including Van Gogh and Marc Chagall [21]. The pigeon's discrimination skills do not stop at only paintings. Pigeons are also able to discriminate between human individuals and have shown a basic understanding of human behaviour [15]. I hope that I have persuaded you not only of the pigeon's ecological importance but also of their intellect and charm.

Concluding Statements

In this article, I have described the ecological importance of only a few species, placing emphasis on those considered undesirable by many people. In truth, all organisms are ecologically important to the functioning of their native habitats. Biologists often use the terms 'keystone species' and 'species engineer' to denote species that appear to be more vital than other species to their respective environments. In my opinion, hierarchical categorisation is impractical in both ecology and the wider field of biology. In research and the application of environmental management, scientists need to stop thinking of organisms as being in an ecological ranking, but rather as part of the highly complex system of abiotic and biotic elements that make up an ecosystem. Nature does not view one animal as inherently 'better' than another, and neither should we.

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Gene-Editing: Where Do We Draw the Line?

Lucas Tan

Since the discovery of Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) in 2012, scientists and pharmaceuticals have invested countless hours and billions into developing ground-breaking gene-editing technologies due to CRISPR's simplicity, affordability, and efficiency [1-2]. The potential benefits of gene-editing through CRISPR range from treating genetic diseases like sickle cell disease[1] and Duchenne muscular dystrophy[2], to increasing the yield and hastening the process of crop growth [3-6]. James J. Lee, a researcher at the University of Minnesota, also claim that, in principle, scientists could utilise CRISPR to significantly boost the expected intelligence of an embryo [7]. For the first time in history, *Homo sapiens* — instead of natural selection — possess the ability to influence the biological fate of living things on Earth. As with any disruptive technology, it is of paramount importance for us to explore the ethical boundaries of CRISPR. Should genetic enhancements such as increasing the intelligence of individuals be allowed? What constitutes genetic enhancements? Where do we draw the line? This article seeks to present existing applications of CRISPR and explore a variety of — but by no means all — ethical concerns regarding gene-editing.

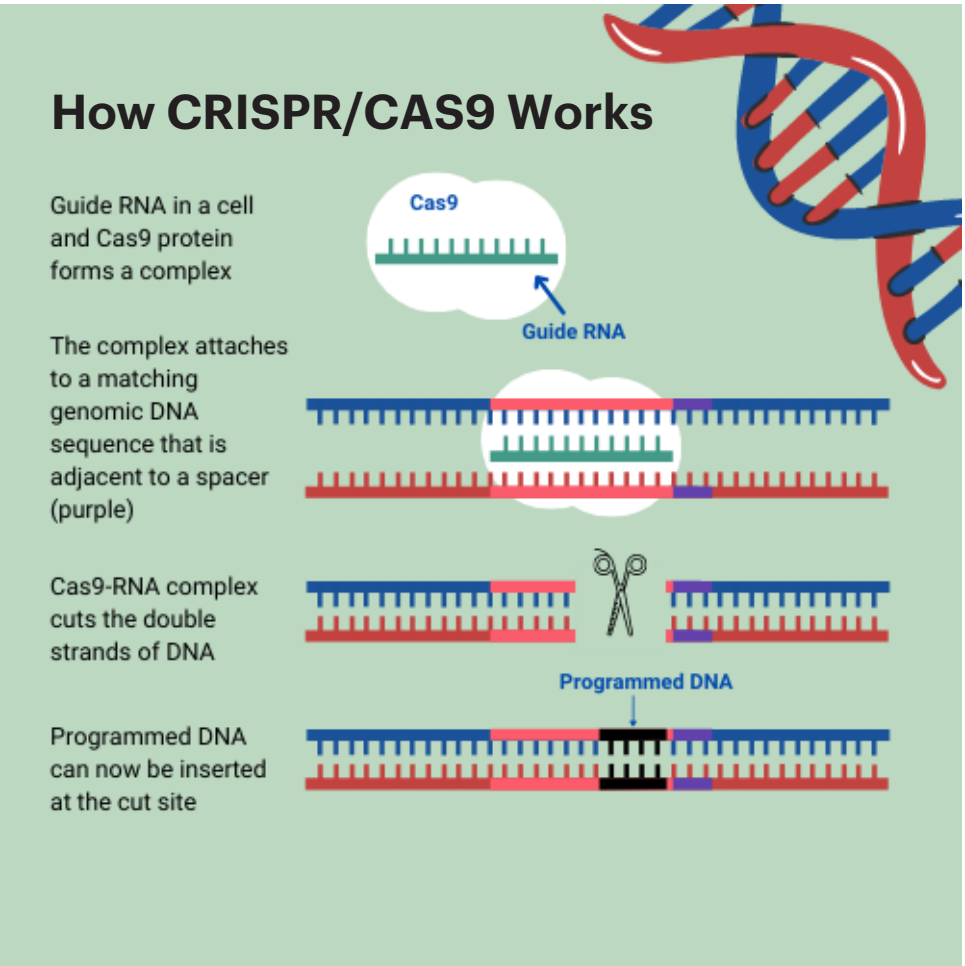

Figure 1: How CRISPR/Cas9 Works adapted from [28].

Before debating the ethics of gene-editing, it would do well for one to understand how CRISPR works. One of the most popular methods scientists use to perform genetic editing is through CRISPR/Cas9. Cas9, a CRISPR-associated protein, is an endonuclease that forms base pairs with DNA target sequences. It accomplishes this by utilising a guide sequence within an RNA duplex, trans-activating crispr RNA (tracrRNA):crispr RNA (crRNA). This enables Cas9 to introduce a site-specific double-strand break in the DNA. Researchers then engineer the dual tracrRNA:crRNA as a single guide RNA (sgRNA) that possesses two critical characteristics: a duplex RNA structure at the 3' side that binds to Cas9 and a sequence at the 5' side that determines the DNA target site through base-pairing with the DNA. This allows Cas9 to target any DNA sequence of interest by changing the guide sequence of the sgRNA programme [8]. Figure 1 is a brief illustration of the process of gene-editing with CRISPR/Cas9.

Genetic congenital abnormalities and disorders are present in 2-5% of births [9], a staggering statistic. Harnessing the power of gene-editing will provide a whole host of benefits. CRISPR gene-editing has already displayed fantastic potential in areas like therapeutics and agriculture. In 2019, D. Alapati et al. accurately timed in utero intra-amniotic

[1]Sickle cell disease is an inherited disorder that occurs due to a single substitution on chromosome 11 which can lead to catastrophic clinical outcomes like chronic inflammation and early mortality [3].

[2]Duchenne muscular dystrophy occurs in ~1 in 5,000 live male births and is an X-linked recessive disease. Most patients display gradual muscle degeneration related to severe muscle weakness, respiratory or cardiac complications, and eventually death, often in their 20s [4].

administration of CRISPR/Cas9 elements—for monogenic lung disease — to an embryonic mouse model through a CRISPR fluorescent reporter system, allowing specific and targeted gene-editing in fetal lungs. Through the process mentioned above, the mouse model, which possessed the human SP gene SFTPCI73T mutations, had enhanced life expectancy by 22.8% and development of lungs, along with decreased pulmonary pathogenesis [10]. More recently, C. K. W. Lim et al. [11] demonstrated that CRISPR possesses the potential to treat Amyotrophic lateral sclerosis (ALS) — remember the ice bucket challenge? Mouse models displayed a significantly decreased rate of muscular atrophy, improved neuromuscular function, and prolonged life expectancy after in vivo base editing [11]. There are also currently multiple ongoing registered clinical trials that utilise CRISPR. One such clinical trial aims to assess the efficacy and safety of genetically engineered, neoantigen-specific Tumour Infiltrating Lymphocytes (TIL), where scientists utilised CRISPR gene-editing to inhibit the intracellular immune checkpoint CISH, for the treatment of gastrointestinal (GI) cancer [12]. Another clinical trial aims to assess the safety and efficacy of allogeneic T cells that were modified ex vivo through CRISPR/Cas9 gene-editing components in CTX130 CD70-directed T-cell immunotherapy, to treat T cell lymphoma [13]. When it comes to agriculture, the benefits of CRISPR are plenty as well. Examples of existing applications of CRISPR/Cas9 in crops include targeting the gene PL or ALC to increase the shelf life of tomatoes and genetic modifications to obtain disease- and virus-resistant plants [14-16]. While CRISPR possesses a host of benefits, it does have its limitations. For example, an optimal CRISPR/Cas tool must attach and/or break a specified target without producing additional off-targets as by-products in complicated genomes [9]. Nevertheless, research work is already underway to enhance the effectiveness and safety of CRISPR technology. In addition to technical limitations, there are multiple ethical considerations to make.

Those most enthusiastic about genetic enhancements call themselves transhumanists. These people believe that we should transcend the blind and arduous process of evolutionary selection since we now possess the ability to control our biological fate [17]. Some, like Nick Bostrom, criticises that idea, claiming that changing our nature will cause us to lose our human dignity [18]. With the development of rapidly advancing gene-editing technologies, proponents of gene-editing claim that if we do not embrace the full potential of genetic engineering, we are denying many individuals of a 'normal' life, and such an act would be considered ethically wrong. Individuals may consider genetic engineering as 'playing God' in various cultures. Others may believe in staying 'natural,' yet with all the processed foods with additives, pesticides, and other chemicals that most of the population consumes daily, what is considered 'natural'? It is possible that gene-editing may eventually become commonplace. Would there then be a stigma associated with not having undergone gene-editing? Could gene edits eventually be associated with certain levels of prestige within society?

Some futurists predict that gene-editing technologies will eventually allow individuals to enhance themselves or handpick traits that they want their children to possess. Many around the world would love physical characteristics like a lower body fat percentage or increased intelligence. It is theoretically possible to intervene with the aesthetics of height, hair colour, eye colour, and perhaps, even the more subtle aspects of appearance and even intelligence [7, 19]. While technologies that can create 'designer' babies are not available yet, they could soon become a reality. A thought-provoking conundrum to contemplate is that when it comes to traits like intelligence, the distinction between genetic enhancements and gene therapy is blurred [17].

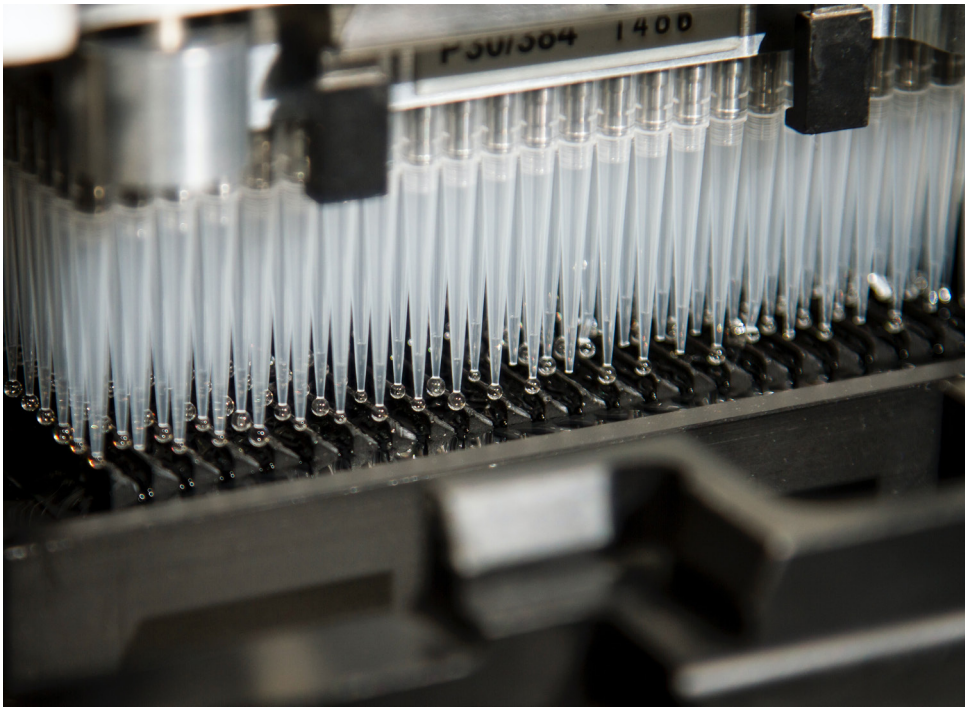

Image by National Cancer Institute from Unsplash

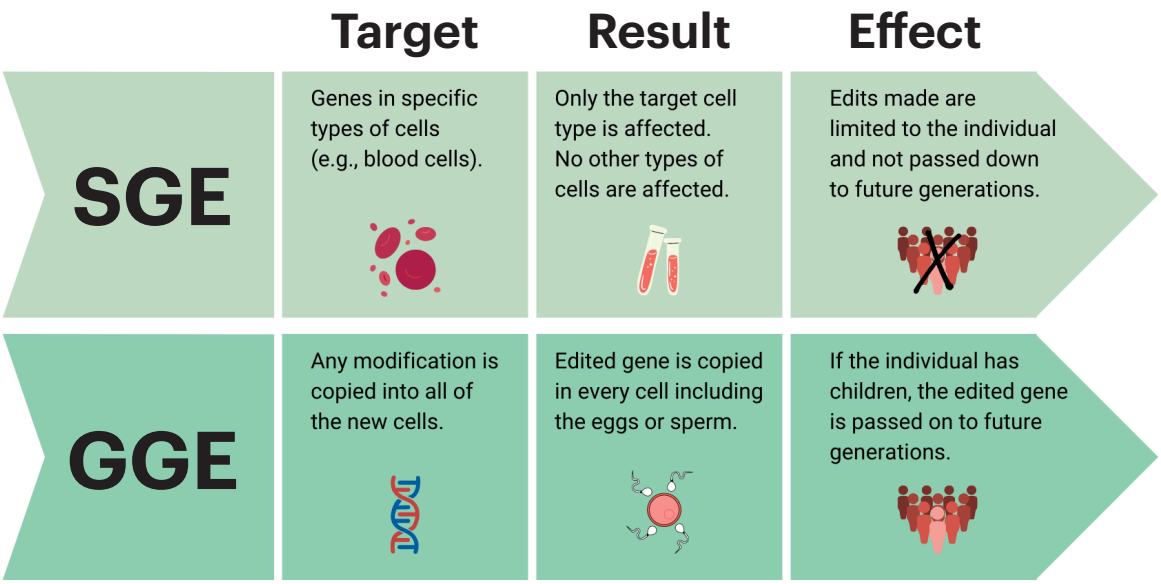

Figure 2: Somatic Gene Editing Vs. Germline Gene Editing adapted from [29].

While increasing an individual's intelligence quotient from 120 to 140 would be considered an enhancement, would raising an individual's intelligence quotient from 90 to 110 be considered therapy or an enhancement? Ultimately, it depends on our distinctions of normality versus abnormality and health versus disease [20]. In a time when self-image and body consciousness is becoming increasingly widespread due to the influence of social media, many—especially the wealthy—will not see any ethical issues with genetic enhancements for aesthetic purposes. Parents want the best for their children. Should they be offered the opportunity to enhance their children genetically, would parents stop at 'gifting' their children an above-average height or increased intelligence, or will there be a never-ending list of enhancements they want? Such a scenario begs a fundamental question: should aesthetic genetic enhancements be allowed, or should we focus solely on gene-editing applications—like therapeutics and agriculture—that bring about societal benefits? Various parties such as policymakers, businessmen, clinicians, and academics need to agree on what constitutes appropriate gene-editing applications in our society.

Aesthetic genetic enhancements raise several concerns. There is a possibility that such enhancements will only benefit the affluent due to cost and accessibility issues, leading to a greater social inequality gap as the rich will get increasingly competent and possess physically ideal traits. Meanwhile, the less fortunate will drift further away from what is considered the new norm. In addition, the approval of aesthetic enhancements could lead to a less diverse society, which may cause us to end up in an environment with less edge, inspiration, and creativity. One thought experiment described by Walter Isaacson to tackle this problem describes two terms: an absolute good and a positional good. Enhanced resistance to common viruses, for example, is an absolute good. On the other hand, enhanced facial features is a positional good [21]. The distinction? Resistance to a virus benefits society, while enhanced facial features give the recipient a positional advantage. Absolute goods such as treating genetic diseases and enhancing resistance to common viruses could lead to happier and healthier individuals. This could translate to increased economic productivity, reduced healthcare expenditure — governments could spend more on other sectors like education — and the possibility of greater equality due to the potential elimination of the biological determinant of health outcomes.

Another grey area that regulators and researchers frequently tread on is the question of somatic gene-editing (SGE) versus germline gene-editing (GGE). SGE only affects the treated patient and specific types of cells. On the other hand, GGE affects all the cells in an organism, including sperm and eggs; hence edited traits are passed onto future generations. Figure 2 illustrates the differences between SGE and GGE. In 2018, a gene-editing researcher at the Southern University of Science and Technology in Shenzhen, China, He Jiankui, implanted edited embryos in a woman. Through CRISPR/Cas9, he disabled the gene, CCR5, that encodes a protein that allows human immunodeficiency virus (HIV) to enter a cell [22]. Recently, the BBC published an article mentioning that Lulu and Nana, the first gene-edited babies to be born, may not actually possess resistance to HIV due to multiple problems with He's methods [23]. The full extent of the consequences of gene-edited babies are still unknown, and He is currently serving a three-year sentence in prison for violating medical regulations [24]. Proponents of GGE cite several benefits. Companies and scientists could utilise GGE to avoid passing on single-gene disorders like cystic fibrosis (CF) — a congenital genetic lung disease that can lead to respiratory and digestive system complications and a shortened life expectancy — especially in cases where two carriers of the gene for CF hope to have a child together. This is because there is a 25% chance that the child of two CF gene carriers will develop CF. Only approximately 19%

of women undergoing IVF produce one viable embryo [25]. In such a situation, in vitro fertilisation (IVF) will not provide any tangible benefit, and GGE would prove more beneficial in preventing CF. In addition, IVF is also unable to select against polygenic diseases such as diabetes and coronary artery disease [26]. GGE could be a powerful tool in the fight against such diseases in the future. On the other end of the spectrum, those opposed to GGE have made multiple arguments, including the safety of individuals who had undergone GGE, the possibility of negative consequences for future generations, whether we are infringing upon the consent and autonomy of future generations, and the fact that we could also utilise GGE for heritable enhancements [25]. As described above, genetic enhancements may not be ideal in our current society due to certain disparities and ethical barriers that may arise, but how society will receive such technological changes in the future is yet to be seen.

To conclude, gene-editing — although incredibly beneficial in numerous ways — brings about a barrage of questions and concerns from governments, academics, and the public alike. There is still a long list of moral and ethical questions that policymakers and researchers — among other significant players — need to discuss and come to a consensus on over the coming decades. One thing is sure: it is imperative for us to ensure equitable access to gene therapies. Everyone should possess an equal opportunity to be in good health, a state of complete social, mental, and physical wellbeing and not merely infirmity or the absence of disease as defined by the World Health Organisation [27]. Prematurely introducing gene therapies without proper regulation, planning and funding could exacerbate existing health inequities, driving increasing differences between ethnic groups and social classes. How society evolves with the advent of gene-editing and where to draw the line between what is permissible and banned — from genetic therapy to genetic enhancements and GGE — is wholly up to us. With the discovery of CRISPR, we possess greater power than ever before, and with great power comes great responsibility.

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Classical Conditioning in *Brave New World*

Sheeta Mo

Science fiction reflects science progress at the time it was written. Authors apply their wild imaginations to scientific breakthroughs to visualise the world of tomorrow. What if we analyse a science fiction masterpiece with real science? Would the description be accurate or outdated? Does it present a possible future of where we are heading? The wonders jumped into my head as I read *Brave New World*. To ease my curiosity, I decided to draw parallels between the novel and *Forty Studies that Changed Psychology* by Roger R. Hock.

Brave New World by Aldous Huxley is one of the world's classic science fiction novels. It depicted a dystopian future of our society where science was used to control people. Biological applications and psychological theories were combined to manufacture citizens into replaceable gears as early as they were embryos. I will focus on the psychological methods used to manipulate people's minds suggested in the book.

Children were conditioned with phobias to fix them in their predetermined social classes. It was done with an extremely unethical approach, by electrocuting and scaring babies in the "INFANT NURSERIES. NEO-PAVLOVIAN CONDITIONING ROOMS" [1, p. 19]. The conditioning wired fear with flowers and books. The fear will last a lifetime to keep lower-class citizens away from literature [1].

"Books and loud noises, flowers and electric shocks–already in the infant mind these couples were compromisingly linked; and after two hundred repetitions of the same or a similar lesson would be wedded indissolubly" [1, p. 22].

It sounds overstated and cruel, but theoretically possible. Let's examine the scene with the Classical conditioning theory of learning. Or you might recognise it as "Pavlov's Dog". It might be the most publicly known psychological phenomenon.

Pavlov identified two types of reflexes: unconditioned and conditioned. No learning is needed for unconditioned reflexes as it is automatic and inborn. In contrast, conditioned reflexes need to be established by learning or experience [2]. In Brave New World, the unconditioned reflex would be fear of sudden loud noises, and the conditioned reflex would be to fear flowers and books. Before conditioning, babies crawled towards flowers and books with "little squeals of excitement" [1, p. 21]. Therefore, the items were neutral stimuli [2]. How did neutral stimuli trigger fear, a conditioned response? The simplest way to explain it is through a diagram:

KEY
UCS: unconditioned stimulus
UCR: unconditioned response
NS: neutral stimulus
CS: conditioned stimulus
CR: conditioned response

Step 1

UCS (loud noises & electric shock) -> UCR(fear)

Step 2

NS(flowers & books) +
UCS(loud noises & electric shock) -> UCR(fear)

Step 3

Repeat step 2 for 200 times.

Step 4

CS(flowers & books) -> CR(fear)

Figure 1: Diagram adapted from the table in [2] to fit with the article's content.

In short, the neutral stimuli were paired with unconditioned stimuli to produce fear. The process was repeated until neutral stimuli became conditioned stimuli. In the end, "the infants shrank away in horror, the volume of their howling suddenly increased" [1, p. 22] when flowers and books were shown to them without electric shocks.

You might think that it was an exaggerated fictional scene based on psychology. Unfortunately, you are wrong. It was almost a direct transcription of the Little Albert experiment carried out by Watson and Ryaner in 1920 [3].

Watson's morally challenged study involved an 11-month-old baby named "Albert B." He was aiming to study how emotions can be learnt. Note that Pavlov's study only focused on reflexes (e.g. secretion of saliva) but not specifically on emotions (e.g. fear). In the experiment, Albert was presented with a white rat and several other fluffy animals and objects. Little Albert was curious, but wasn't afraid of the objects. Then, a white rat was shown to him

again while striking a steel bar to make loud noises behind the baby. Albert was frightened and started crying. The experiment was repeated seven times [3] until little Albert cried and clawed away at the sight of a white rat, even when there were no loud noises [4].

Further observation of Albert showed that conditioning could be generalised, transferred between situations, and persist over time. It meant that Albert was fearful towards not only white mice but also rabbits, fur coats, and even a Santa Claus mask [4]. His fear was not limited to the lab environment. Rather, it happened when Albert was taken to another room. The conditioned emotional response stayed over time, as little Albert was afraid of the same items even after a month of no experiment [3].

Putting it in *Brave New World*, the babies were likely to fear all flowers and books even if the objects had different features. They would be afraid no matter what environment they were in. It was also possible that they would stay conditioned for a lifetime (especially when there is nothing else in the society to 'recondition' them).

"They'll grow up with what the psychologists used to call an 'instinctive' hatred of books and flowers. Reflexes unalterably conditioned" [1, p. 22].

So why is this important? Fictional works are stories after all. However, we should be alarmed if the story sounds too much like real life.

After examining the fictional scene in *Brave New World* with real psychology, we come to two conclusions:

a) It can be done.
b) It had been done.

Science fiction is fascinating and frightening because the future it visualises could be true. Huxley wrote the novel because he saw trends in our society that might lead us to a similar world where science is manipulated to control and exploit individuals. Conditioning people for control might not be as extreme as Huxley envisioned. It might be done subtly for 'harmless' reasons. For example, linking a product with positive emotions to maximise the effect of advertisement.

Science fiction is like a fire alarm. It screams sharp warning when there is any trace of smoke. We might never get a fire, but we all need an alert in our hearts. Hopefully, it never rings.

Sheeta Mo - BSc, Biomedical Science

We often mention science and art as opposites. Yet, I think science is poetic. When I look up at night, I see every star following Newton's law with grace, knowing they are the same stars Van Gogh gazed at once. I want you to see the world with my eyes.

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Pinpointing breast cancer from a bioengineering perspective

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Fun Fact

You can fit every planet in the solar system
in the distance between the Earth and the moon.

Closing Comments

That concludes the first issue of Volume Two. An enormous thank you again to all our contributors, readers, and to the people who make this publication viable. We're a long way from the front cover back here, but take another look at the wonderful original artwork by marketing coordinator Aimee. The overall design of the magazine is put together by Gene, our creative director, and he continues to blow us away.

This issue also marks the first time we use our brand new ISSN number, uniquely identifying us as a serial publication. As always, we welcome new writers, and outreach is ongoing. Get in touch if you have an idea!

Best wishes and happy studying,
The Scientific Executive Team

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