βluesci

Cambridge University science magazine

The Cambridge University science magazine from
VARSITY
Easter 2014
Issue 30
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FOCUS
Cognitive biases

Blood types • Optical illusions • Quantum computing
Super-foods • Discrimination • Frederick Sanger

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Bluesci About Us...

BlueSci was established in 2004 to provide a student forum for science communication. As the longest running science magazine in Cambridge, *BlueSci* publishes the best science writing from across the University each term. We combine high quality writing with stunning images to provide fascinating yet accessible science to everyone. But *BlueSci* does not stop there. At *www.bluesci.org*, we have extra articles, regular news stories, podcasts and science films to inform and entertain between print issues. Produced entirely by members of the University, the diversity of expertise and talent combine to produce a unique science experience.

Issue 30: Easter 2014

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The Human Machine

UNDERSTANDING HOW OUR BRAIN WORKS is one of the most complex puzzles of our time. Just last year the president of the United States, Barack Obama, unveiled a $100 million initiative to "unlock the enormous mystery of the human brain". Formed by a hundred billion nerve cells, and united through a hundred trillion interconnections, our brain is what defines us as a species and as individuals. It is in charge of all we feel, think and do. In Issue 30 we have taken human cognition as our main theme.

How many times have you made a choice between restaurants or political candidates? How certain are you that you're making objective decisions? In our focus article we review some cognitive biases in human decision making and account for the effects they can have upon our daily lives. In a second article we refer to another type of bias, the psychology behind racial discrimination, unfolding how it is rooted in us. Although it may feel frightening to know the extent of this bias, it is only through awareness that we can overcome it. Finally, we discuss another aspect of human cognition: the tricks our mind can play on us through optical illusions.

Many other subjects also draw our attention on this Issue We explain why parasites can have a different effect on people according to their blood type, review the recent outbreak of a virus that has unsettled the Middle East, account for the evidence behind the popular belief that vegetables in our diet have positive effects upon our health and describe how hundreds of animals use body movements to communicate. We also refer to some of the front-line technology that is revolutionising the world we're living in: we explain how quantum computing works, and discuss the possible outreach of stem cells therapies.

We also celebrate the lives of two extraordinary figures that have shaped the modern world: The British biochemist who taught us how to read the code of life, Frederick Sanger, and the South African philanthropist Nelson Mandela. Both men were born in 1918 and died late in 2013.

This Issue is the product of the joint effort of dozens of people. Both authors and editors have very different academic backgrounds. It is thanks to this diversity that we find a great mixture of topics and perspectives across the Issue. If you would like to be one of the people contributing to this magazine we're always looking for people to get involved in *BlueSci*.

Ornela De Gasperin Quintero

Ornela De Gasperin Quintero
Issue 30 Editor

Open Access

Sarah Smith discusses the advantages of open access images

THE MEMBERS OF *BLUESCI* dedicate many hours to choosing interesting and appropriate pictures to complement the articles in the magazine. This process involves selecting pictures that primarily represent the author's writing, but other factors are also considered. The images must be at a high enough resolution (300 dots per inch (dpi)) so that they're not pixelated upon printing, and must be changed into CMYK colour to ensure that the ink does not smudge on the glossy paper. But most importantly, all the images used in *BlueSci* are available under Creative Commons licences, either the Attribution (CC-BY) licence or the Attribution-NoDerivs (CC BY-ND) licence.

If you look carefully through the magazine, you will see that every image is accompanied by a vertical reference giving credit to the owner of the image–this is one of the rules of all the licences. The image can be shared (redistributed in any medium or format) and adapted (remixed, transformed, and built upon–CC-BY only) as long as the appropriate credit is given to the owner. The magazine is also required to provide a link to the licence (see the small print on page 2!).

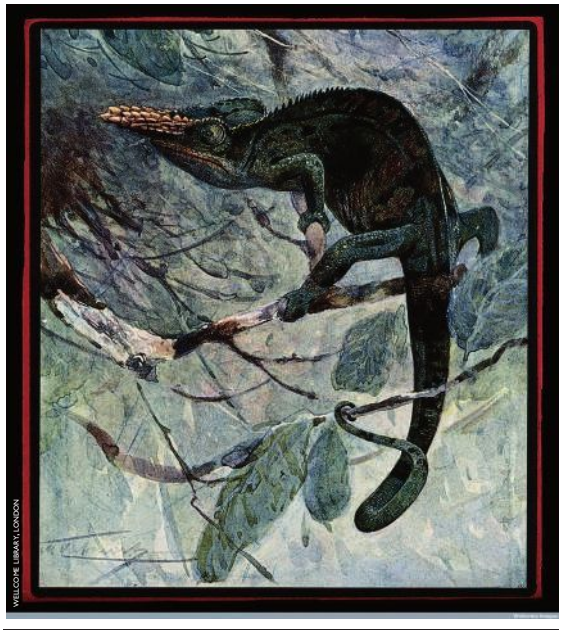
BlueSci often relies on photographs taken by members of the public that are uploaded to Flickr under these licences, or those available on Wikimedia. However, several large institutions such as the Wellcome Trust, NASA and the British Library promote an open-access attitude to images. The latter of these uploaded over 1 million images to Flickr, including 65,000 books, diagrams and maps.

In January of this year, the Wellcome Trust Library made over 100,000 high resolution images from its vast archive freely available through the CC-BY licence. This enormous collection includes manuscripts, paintings, etchings, early photography and advertisements, all revealing the interesting and often macabre world of historical medicine and health-care.

The image on the cover of Issue 30 is one of these newly-released images. 'In Memoriam' is a relatively modern acrylic painting by Richard Ennis, a school Art teacher based in Sonning. It was painted in 2001 and hung in the school hallway, until it was purchased by the Wellcome Collection in 2013. The portrait was painted as a memorial to a friend of the artist, who died of skin cancer that affected the lip and face. Rather than painting a traditional *memento mori* (Latin for 'remember that you will die'), Ennis consulted several pathologists about the complex layering of tissues in the face and visited the Museum of Zoology and Natural History, in Florence, which is famous for its collection of wax anatomical models. The result is the detailed acrylic painting showing how complex and beautiful the tissue interactions of the human body can be.

The rest of the collection encompasses the same desire to explore our own physiognomy, minds and culture through art and observation. From the oldest piece in the collection, an ancient Egyptian prescription written on papyrus, to satirical images by caricaturists like George Cruikshank, which mock the medical profession, to 20th century adverts for the kitchen cleaner 'Vim Cleanser and Polisher'.

Without copy-right owners providing access-channels to these images, by releasing them under Creative Commons licences, not-for-profit organisations like *BlueSci* could not afford to include pictures in their publications. So the next time you take a picture and upload it to Flickr, remember to consider the licencing–release it to the world and your image could end up in a magazine just like *BlueSci*.



One of the images released by the Wellcome Trust: a 1926 painting of a chamaleon

Sarah Smith is a 4th year PhD student at the Wellcome Trust Sanger Institute

All 100,000 images can be found at wellcomeimages.org and details of creative commons licences can be found at http://wiki.creativecommons.org

News

Bacteria solution to biofuel problem?


PATRICK NOUHAILLIER

CURRENTLY ABOUT 1 IN 7 people worldwide are chronically malnourished and, with the global population predicted to increase to 9 billion by 2050, food security is a hugely important issue. However, vast areas of viable agricultural land have already been, and will continue to be, converted for bio-fuel crop production, especially as oil prices continue to rise. Now, recent research appears to have discovered a potential new approach to developing biofuels quickly, using a method that doesn't require large scale land conversion. It looks like bacteria could once again save the day. *Streptomyces*, a type of bacteria, can make and store large amounts of oils called triacylglycerols (TAGs), which are used in the production of biodiesel. Fortunately, as this versatile bacterium has been used extensively by the pharmaceutical industry to produce life-saving antibiotics, we already know how to grow it in huge amounts. The research, led by Deniset-Besseu's team from the Université Paris-Sud, investigated how *Streptomyces* store TAGs. Using a novel instrument that combines an atomic force microscope with an infrared laser source, the team was able to identify the types of strains that accumulate lots of oil and those that store very little. Hence they were able to identify which strains might be the most productive to harvest. Furthermore, the researchers claim that their technique could greatly speed up the identification of other microbes that could also produce large amounts of bio-oil. Although biofuels will continue to be grown in the conventional way across the world for some time to come, this research does offer an exciting new avenue to be explored in the quest for both sustainable fuels and food security. **ZBH**

Check out *www.bluesci.org or @BlueSci* on Twitter for regular science news and updates

Cancer treatment clogs circulation

ALTHOUGH CANCER PATIENTS are commonly treated with therapies that reduce the growth and spread of tumours by preventing the growth of tumor blood vessels, it has recently been shown that these 'anti-angiogenic' agents used in cancer patients prevent the natural dissolution of inappropriate venous blood clots (thrombi). If these thrombi persist, they can lead to debilitating symptoms such as leg pain and ulceration, or detach and lodge (thromboembolise) in vital organs including the lungs, heart and brain. This can result in pulmonary embolism, myocardial infarction and stroke, respectively. In their study published in *Arteriosclerosis, Thrombosis, and Vascular Biology*, authors from King's College London and the Department of Physiology, Development and Neuroscience at the University of Cambridge showed that anti-angiogenic treatments slowed the already gradual process of organisation by which venous thrombi are naturally removed from the circulation. Given that venous thromboembolism is responsible for more deaths in the UK than breast cancer, road traffic accidents and HIV combined, and that cancer patients are approximately five times more likely to suffer from venous thromboembolism than non-cancer patients, authors concluded that "the pro-thrombotic effect of anti-angiogenic agents should be taken into consideration when managing the complications of venous thromboembolism in these [cancer] patients". It is clear that the balance between therapeutic benefits and harmful side-effects should be carefully considered when treating cancer patients. While improved life expectancy and quality of life are the primary goals of most health-care treatments, this study highlights the importance of being aware of their possible consequences. **CE**

NASA puts a guiding ARM around the shoulder of asteriods


MARCVAN NORDEN

NASA ARE DEVELOPING an Asteroid Redirect Mission (ARM)–the first of its kind, in order to protect our planet from possible impacts. Near-Earth objects (NEOs) are interstellar debris that, thanks to the gravitational pull of our planet, have the potential to enter our atmosphere. One such NEO did just that in February of last year, and exploded over Russia with the force of a large atomic bomb.

Tracking NEOs is not a new development, but ARM will work alongside technologies currently in development for sending humans to Mars in order to identify, capture and subsequently redirect candidate asteroids. Currently, NASA are working on two concepts: the first will capture and redirect a small asteroid, the second will retrieve part of a larger asteroid and then return it to a lunar orbit.

It is estimated that dozens of small (20-40 foot) asteroids fly past Earth every year that could be possible candidates for ARM, though these foreign bodies don't reflect much sunlight, making them hard to spot. Currently, huge radar telescopes–some hundreds of feet wide–are needed to determine the size, rotation and destinations of these asteroids. Currently, roughly half of these are masked by the glare of the Sun. To aid their search, NASA have reactivated their NEOWISE spacecraft and are upgrading the detection capabilities of their telescopes. These developments don't come cheap though, and NASA's 2014 budget includes $105 million for the redirection of an asteroid, and to increase innovative partnerships and approaches to track and mitigate these potential threats. **J-MH**

Reviews

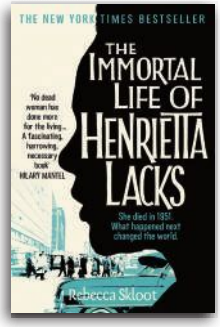
This Week in Virology - Vincent Racaniello

THIS WEEK IN VIROLOGY (TWIV) is a weekly 90 minute podcast presented by virologist Vincent Racaniello, Professor at Columbia University. Racaniello discusses either cutting-edge developments in virus research or the basic tenets of virology, with regular guests including Dickson Despommier, Alan Dove, Rich Condit and Kathy Spindler, plus a carousel of other famous virologists. The podcasts, which began in 2009, are aimed at a general audience regardless of their science background. Each episode reviews topical scientific papers that have been recently published, and the presenters explain any complex scientific terms along the way. The result resembles a conversation between friends down the pub–beginning with a chat about the weather across the globe, but then quickly turning to topics such as vaccination and science policy. Each episode is capped with alternative forms of science outreach ranging from Youtube videos of Chris Hadfield singing in space to blogs selling woollen virus models. Whether you're an arts student with a passing interest in science or a scientist from a different field, you'll find something that will capture your imagination listening to TWiV. **SS**

Radiolab - Jad Abumrad and Robert Krulwich

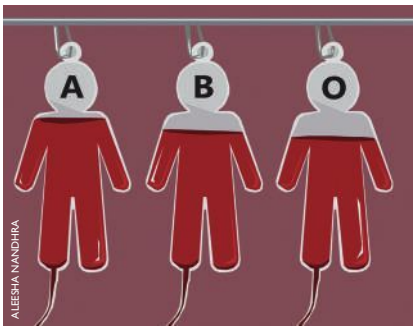
HAVE YOU EVER WONDERED whether other animals laugh as we do? Can you think of a woman whose skin and blood DNA don't match? Could you imagine that parasites may be able to cure our allergies? Jad Abumrad and Robert Krulwich tackle these and hundreds more questions in a science podcast that brings together laughter, emotion and wonder. Radiolab is broadcasted by WNYC, a public radio station from New York. Each episode attacks a topic from three different perspectives, exploring them using anything from experiments and interviews, to stories, and usually finishes without giving conclusions, leaving questions open for the public to reflect on. Jad and Robert manage to discuss complex topics in an easy and unthreatening way, creating a fun environment throughout the podcasts. They laugh all the time, continually challenge each other's arguments, and openly acknowledge to not always understand what their interviewees are saying. On top of that, Jad, who initially intended to work as a composer, incorporates great sounds throughout the episode. Radiolab has received several awards, including the National Academies Communication Award, and currently has more than a million and a half listeners. It's easy to see why–the show's incredible stories always leave me amazed, while its jokes have made me laugh so hard I've tripped off the treadmill! **ODG**

The immortal life of Henrietta Lacks - Rebecca Skloot



Pan MacMillan, 2010

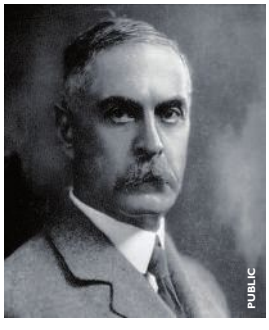
THE IMMORTAL LIFE OF HENRIETTA LACKS is a powerful non-fiction work that touches on subjects ranging from the development of scientific techniques such as cell culture, to race and class issues in America in the 1950s, and the impact of these issues today. In this book, Rebecca Skloot explains the origin of the famous HeLa cell line. She does so by piecing together old medical and laboratory files and speaking to those involved; a challenging feat since many records have been lost and many of the people involved have passed away. In addition to explaining the science behind this achievement, Skloot tells us two stories, one about her journey searching for the facts, and another about the history of the Lacks family. HeLa cells originally came from a tumour in the womb of a black, lower class woman named Henrietta Lacks taken during a biopsy without her consent. They were given to researchers who were attempting to culture the first human cell line. The discovery that Henrietta's cells could grow in the laboratory led them to track down and visit the family repeatedly, without properly explaining the research being done. The experience impacted the family and fuelled the injustice felt by them, especially in light of the massive profits made by companies selling these cells. The number of scientific discoveries achieved thanks to Henrietta's cells is massive–over 60,000+ papers have been published using the cells. The history surrounding this scientific achievement and the examination of the issues surrounding this case make for a compelling read. **CS**



ALEESHA NANDHRA

Blood Groups and Infection

Sarah Caddy discusses how your blood type can alter your susceptibility to infectious diseases


PUBLIC

Dr Karl Landsteiner discovered the different blood groups in humans

RED BLOOD CELLS ARE coated in a set of carbohydrate molecules. Before the turn of the 20th century, these seemingly innocent carbohydrates were responsible for many deaths following blood transfusions. This is because the carbohydrates on red blood cells characterise the blood groups, and blood group matching is essential for safe blood transfusions. But what are blood groups and how are they associated with infections?

In 1900 Dr Karl Landsteiner discovered the different blood groups in humans-A, B and O. Dr Landsteiner showed that mixing blood from an A-positive and a B-positive person caused disastrous clumping or 'agglutination' of the blood in a test tube. This discovery finally clarified why some blood transfusions were fatal.

Subsequent work elucidated the mechanisms behind these dramatic reactions. All red blood cells are O-positive by default and it is the presence of a specific enzyme, either an A or B enzyme, that dictates whether an A or B sugar will be added to the core carbohydrates that coat red blood cells.

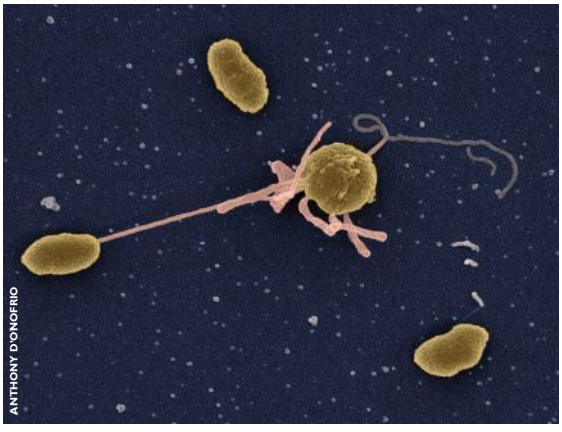
Agglutination of red blood cells occurs when antibodies (immune proteins that recognise and help destroy harmful molecules) target foreign blood group carbohydrates. Antibodies against foreign blood groups naturally develop in humans. However, the immune system of an A-positive individual will not allow the production of antibodies that target A sugars. In other words it will not recognise its own cells as foreign or threatening. Similarly, in a B-positive individual no anti-B antibodies develop. If someone's blood group is O, their immune system will make both anti-A and anti-B antibodies. If someone with an O-positive blood type is transfused with A- or B-positive blood, their antibodies will destroy these new red blood cells. In 1 out of 20 cases this leads to sudden death.

But why do the different blood groups exist? Is there a benefit in having different blood types?

Exactly why there is a mixture of different blood types in many species is indeed a mystery. One hypothesis is that pathogens may have played a role in the evolution of blood types. Many pathogens use carbohydrates from the cell surface as receptors to bind to the cell. Receptors can also be used as anchors to prevent from being swept away and they might help a pathogen enter the cell or release its toxins inside it. Depending on their blood type, people are more or less susceptible to certain pathogens. If you do not express a pathogen's receptor but your neighbour does, you will be safe from infection but your neighbour might fall ill.

Cholera was the first infectious disease shown to affect people in different ways according to their blood group. The responsible bacterium, *Vibrio cholerae*, causes severe watery diarrhoea and can be fatal if appropriate treatment is not received. Outbreaks in the developing world usually have devastating consequences, as happened in a recent epidemic in Haiti, which resulted in over 8,000 deaths.

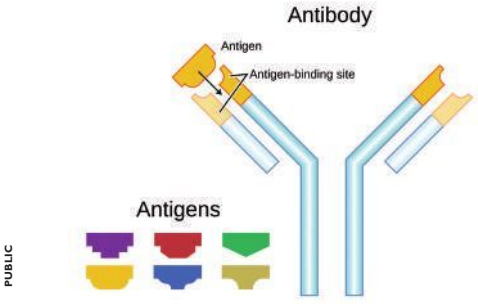
In the 1970s researchers noticed that individuals with blood group O were more likely to become infected with cholera than people with blood group A or B. Because *V. cholerae* is a bacterium that causes infection in the gut, the fact that blood groups mattered was a mystery.


ANTHONY D'ONOFRIO

The bacterium that causes cholera has a higher incidence in people with blood type O

It turned out that A, B and O antigens are not only expressed on red blood cells. They are also found on epithelial cells, including those lining the gut. A more accurate term for these carbohydrates therefore includes the prefix 'histo', meaning tissue. These antigens are found in the gastrointestinal tract of many different animal species, but only humans and great apes express the histo-blood group antigens on the surface of their red blood cells.

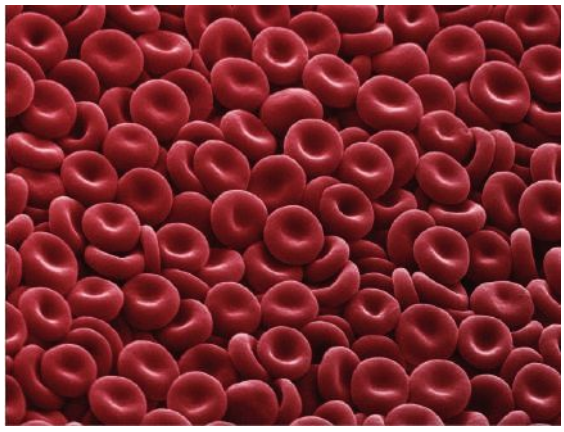
Once the properties of histo-blood group antigens were understood in more detail, an association between cholera infection and blood groups could be explained by focusing on the carbohydrates present in the gut. The current theory is that A and B carbohydrates on the cell



surface block the binding of the cholera toxin to its receptor molecule, ganglioside GM1, which is also located on the cell surface. People who do not have A or B carbohydrates on their cells cannot disrupt this interaction, and hence the cholera toxin enters the cell and causes disease.

People with blood group O are at an evolutionary disadvantage in a cholera-endemic region. This may explain why the proportion of O-positive people in such areas is significantly smaller than in parts of the world where cholera infection is very rare. If a person dies from a cholera infection, they cannot pass on the O blood group to their offspring and hence the proportion of O individuals decreases. This suggests that the blood group distribution in host populations can be substantially altered by pathogenic threats.

For a long time, researchers had suspected that the carbohydrates that determine blood groups could enable pathogens to enter cells, not merely their toxins. In 2002, the first pathogen that uses receptors in this way was finally identified. Human norovirus, the cause of the winter vomiting bug that infects up to three million people in the UK every year, was shown to bind to blood group carbohydrates and enter the cell. The first norovirus strain studied turned out to bound strongly to A and O blood groups, but less efficiently to B. This led to the hypothesis that people with B blood



Human red blood cells are coated by carbohydrate molecules which determine the blood type

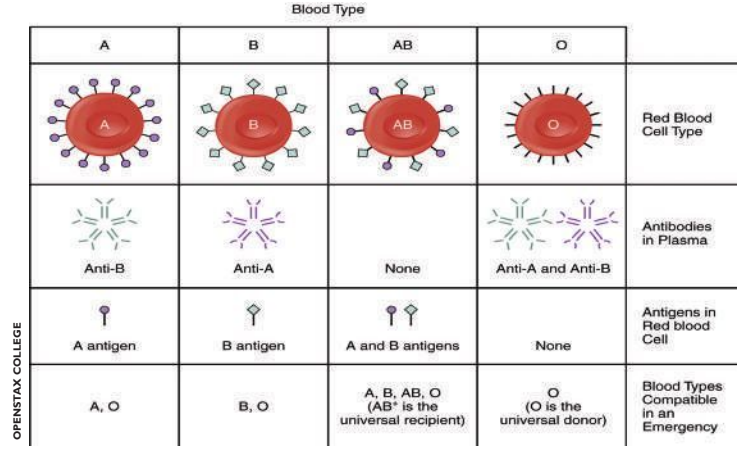
group would be less susceptible to the disease, a hypothesis that was confirmed shortly afterwards.

Many other strains of noroviruses have now been studied, and all of them can recognize at least one of the A, B and O blood group antigens. Interestingly, the strains that have emerged more recently are able to bind to the three blood groups. The most prevalent norovirus strain in the world today is known as GII.4, which can recognize virtually any blood type. This suggests that pathogens can evolve to encompassing a broader host number.

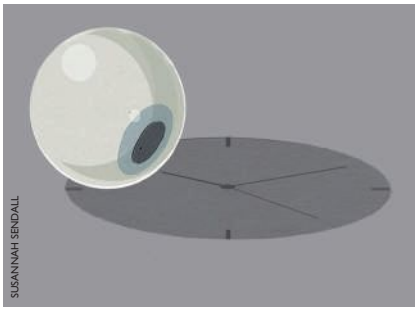
As well as *V. cholerae* and noroviruses, additional pathogens are now regularly being identified that interact differently according to their hosts' histo-blood group. These include *Escherichia coli*, rotaviruses and the dengue virus. Each pathogen attacks blood groups in slightly different ways, which means that in a world full of different infectious diseases, eradication of a single blood group is very unlikely to happen. Unless we find a way to conquer all the blood group-associating pathogens, we will have to keep checking blood types thoroughly prior to blood transfusions for millennia to come.

Agglutination occurs when antibodies recognise foreign red blood cells

The carbohydrates on the surface of red blood cells determine what blood type you can receive



Sarah Caddy is a veterinary surgeon and a 3rd year PhD student at the Division of Virology



Eyes See?

Robin Lamboll explores the unconscious side of sight

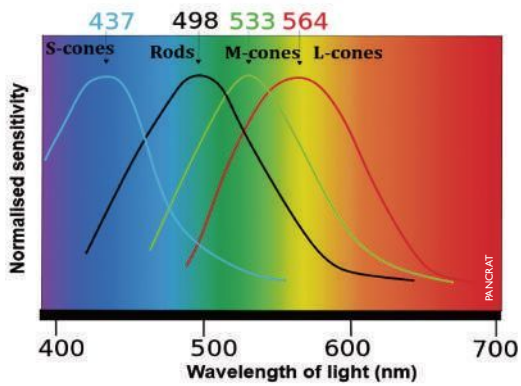
WE NORMALLY ASSUME that our eyes work in much the same way as a video camera, and as far as light works, that's true. Light enters through the pupil and is focused on a range of specific light-sensing cells in the retina. However there are several evolutionary quirks in the retina's layout. That means that making an image out of the light that hits it requires a lot of guesswork from the brain.

For instance, we generally think that our eyes send our brain continuous images of the world in front of us, however much of our vision is based on assuming that things stay the same unless there's evidence to the contrary. One type of light-sensing cells, known as rod cells, are responsible for most of our peripheral vision. These cells only notify our brain when there are significant changes in the light intensity they receive. The other type of light sensitive cells, called cone cells, are responsible for our central vision and can quickly lose sensitivity to a continuous signal. We're familiar with the after-effects of looking at a high-contrast picture or a bright light being temporarily 'burned' into our retinas, but this happens to some degree with all images. To keep our sight sharp, the eye has to keep changing precisely where it looks, a motion that goes on subconsciously even when staring at something.

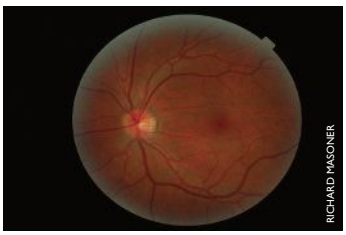
These factors are thought to be behind the apparent motion of several optical illusions; slight movements of the eye will make the after-effect image overlap with different parts of the current image. When the two are superimposed, you get a complicated resultant image where some parts have overlapping similarities and other parts have overlapping differences. If one pattern moves relative to the other even a little, these areas of overlap change, giving the appearance of motion.

The slight shifting of focus by the subconscious when looking directly at something is known as 'fixation', but the subconscious controls several other ways of moving the eyes too. The eyes can continuously track a slow-moving object, but can't move smoothly unless there is something for them to follow. If there isn't anything to follow, or if the eyes need to move faster, they make sudden jumps known as 'saccades'. You can see this by looking at your finger as it makes a circle in front of you and trying to follow an imaginary circle. During a saccade, the eye moves as fast as it can, but once it has started, it can't be stopped. Although saccades can be started consciously, they are controlled subconsciously. During a saccade, there is no 'seeing' done–the images change too fast, and the brain only processes the signals coming from the eye to see if they have settled down yet.

This temporary blindness is why you can't see our own eyes move when looking in a mirror. It's also the explanation behind the stopped-clock illusion. When you look at a clock, the time before the first second passes often seems longer than the time between other seconds. This is impossible: surely it should be shorter as you only started looking at the clock some way into the second. It's because we add the time it takes our eyes to reach the clock to the time we think we've been looking at it. Our brains construct the illusion of continuous experience by filling in the gap of the saccade with what we see



A sketch of how cones and rods are sensitive to different wavelengths of light



The retina is the region of the eye where our light-sensing cells are

after it has finished, so this phenomenon seems to last a little longer than it really does.

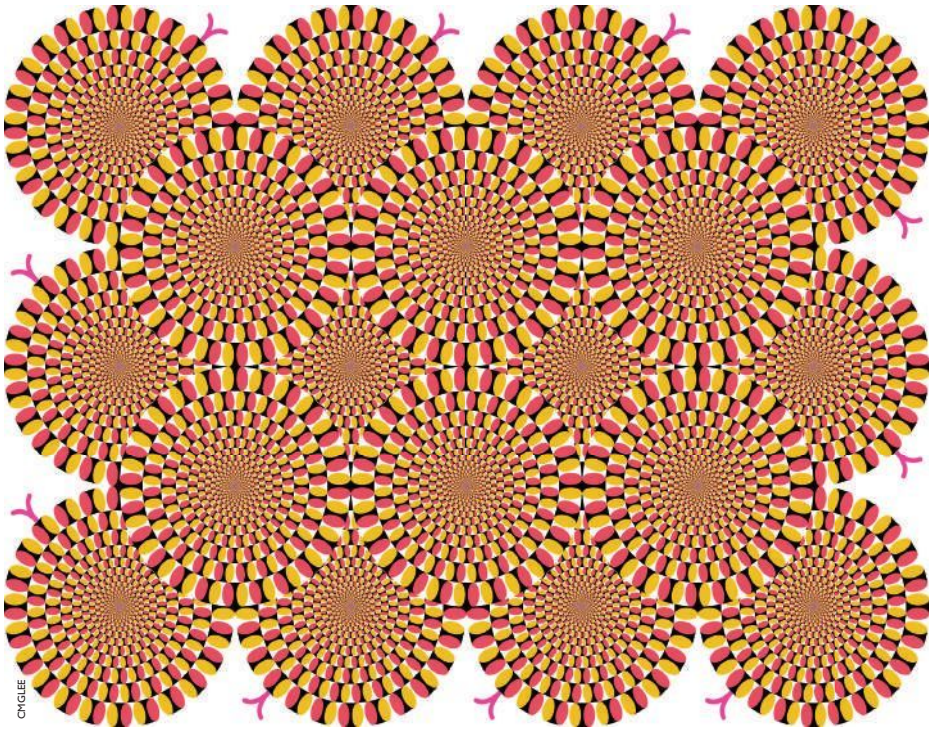
Experiments using eye-tracking software that starts timing when the eyes begin to move show that people think they have been looking at the clock a few milliseconds before the saccade starts. However the illusion does not work if the clock is moving relative to the person, either if the eyes are fixated or in a saccade, as the brain does not know what to fill the gap in with. In these cases, people accurately judge how long they have been looking at the clock.

But why can't we read the clock face unless we look directly at it? Why do we have to have things in the centre of our vision in order to read them? The answer goes back to the two types of light sensitive cells in the eyes, the rods and cones. Most cone cells are found directly behind the pupil, in a region of the retina called the fovea. They're densely packed, which means the sight can resolve small details, which is needed to read. The number of cones drops off steeply away from this spot, to be replaced with rod cells. Rod cells are more sensitive to low levels of light, but respond to light slightly slower than cones. They are more loosely packed and generally several rod cells will send information to the same neuron, so the signal from these cells is much less precise than the signals from cones. This means it is increasingly difficult to make out detail away from what we're looking at. Interestingly, it also means that we can't make out the colour of things in the corner of our eyes. The perception of colour outside the centre of our vision is largely reconstructed from memory, as all rods are only sensitive to the same part of the spectrum.

Cones come in three types that are most sensitive to short, long or medium wavelengths of light, and are therefore known as S-L-or M-cones. By comparing how the three types of cones are activated right next to each other, the eye can make out colour in the fovea. For unknown reasons there are considerably fewer S-cones (blue-sensing) than L-or M-cones, and they are also more spread out throughout the eye. This means that people are less capable to work out fine detail in blue, but that blue colour can be sensed further away from the centre of vision. You may also notice that the S-cone sensitivity on the graph is cut off around 400 nanometers, which is the range of visible light. This is not because it isn't sensitive to ultraviolet light–in fact the two other types of cones should show a small peak there too–but sensitivity there doesn't matter as the lens in the eye absorbs the ultraviolet light. People who have had their lenses removed for medical reasons can see 300-400 nanometers of light, which they report as whitish blue.

Because the eye works with three colour-specific cones, we can't necessarily tell the difference between green light and a combination of yellow and blue light that stimulates the cones in the same ratio. Most colour technology relies on this fact–computer screens and printers can only produce three different colours and make up a rainbow by varying the relative amounts of them. However we also need a way of reporting combinations of light that don't correspond to anything on the rainbow, such as red and purple light together. This is how we make pink light. Pink, like white and black, isn't a pure colour found in the rainbow–it's one of the few signs our eyes give us that most of what we see isn't just one wavelength of light.

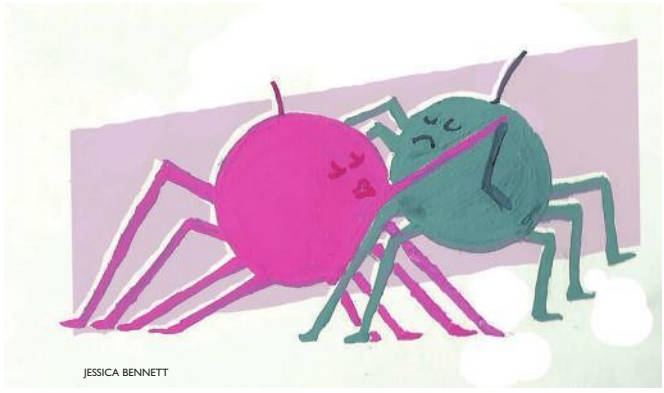
Our brains usually give the impression that our eyes see exactly what's going on in front of us all the time. In reality, a lot of perception is done in the brain, processing the information from the eyes and combining it with previous information, filling in the many blanks with assumptions. Normally the assumptions are good, so good that we don't have to notice them. But knowing they are there, how amazing it is that we can make sense of the world at all.



This optical illusion makes us think that the image is moving

When you look at a clock, the time before the first second passes seems longer than the time between other seconds

Robin Lamboll is a 1st year PhD student at the Department of Physics


JESSICA BENNETT

Shake It!

Caroline Fabre invites you into the world of body language in animals


K.ALDARI

The jumping spider performs a dance during courtship

HOW MANY TIMES have you shaken your body in a club or a disco? Are you bewitched at the sight of a good dancer, performing on the dance floor or in the TV show 'Strictly Come Dancing'? Does body shaking fascinate you as it does thousands of people? Indeed, the term 'body shake' results in about 660,000 hits on YouTube (which these days seems to account for what's in Vogue). And I'm sure you will agree that 'shake/move your body' are probably the most repeated lyrics on dance floors. In Michael Jackson's song 'Shake your body down to the ground', these words are repeated around 20 times in the course of three minutes.

We humans tend to think we have the monopoly for shaking our body to the sound of rhythmic music, which, let's face it, we often do in the hope that our debonair moves might impress or seduce others. But are we actually the only species in the world whose social life involves sometimes 'rocking their bodies'? The answer is no. Many animals shake their bodies in a similar fashion to court potential mates or to impress the competition. So we didn't invent it. And what's more, by shaking their bodies 'down to the ground', animals can even produce the beating music that goes with the shaking.

Spiders appear to use body shakes a lot. The work of Damien Elias and his colleagues at the University of California, Berkeley, describes the how and why behind the peculiar movements of the jumping spider, *Habronattus dossenus*, during courtship. The astonishing performance of the courting male cannot leave you insensitive to his charm. The male shakes his body in a flamenco-like manner, to convince the female to copulate with him. The female is attentive to his performance, and if his dance is good enough, she will become receptive and choose him for mating. Before this study was published, the general belief was that spider courtship relied only on visual cues to 'check out the male'. However, Elias' study was able to show that the male is in fact performing more than just body moves. In addition, his shakes produce vibrations in the ground that the female can perceive. So the female is not only looking at the male, she is also sensing the vibrations on the dance floor. In a way, the male spider's flamenco dance is all-inclusive, and it includes the castanet effect.

Many insects can also move their bodies to 'show off'. Recently, a group of scientists in the Department of Zoology at the University of Cambridge were surprised to discover that male *Drosophila melanogaster* (the flies that appear on your fruits if you leave them out for too long) also shake their bellies during courtship. These tiny abdominal shakes make little vibrations in the ground that can be perceived by the female, and indeed help attract her for mating. Many scientists have used these flies to study various biological processes for decades, yet few would have expected that these insects were 'belly dancers'.


FURT WANGLI

Fruit flies also shake their bellies during courtship

Spiders and flies, however, are not the only 'Lords of the Dance' on Earth. When looking at animals that are closer to us in evolutionary terms, researchers found that they also use body shaking in social contexts. For example, Michael Caldwell and his colleagues at Boston University found that red-eyed tree frog males vibrate their whole body to impress

Male red-eyed tree frogs vibrate their whole bodies to intimidate rivals

and intimidate fellow males on the same plant. Again, they found that these body movements convey aggressive signals by eliciting vibrations in the stem of the plant, the frog's competitive 'dance floor'.

What about bigger animals, who may need to communicate over much greater distances? The work of O'Connell-Rodwell and her colleagues at Stanford University has shown that both Asian and African elephants, the biggest mammals walking on Earth, communicate using vibrations on the floor over distances of up to 20 miles. To 'shake the ground' and produce these gigantic vibrations, elephants do not need to wriggle about as much as smaller creatures–foot stomps are more than enough. The signals generated seem to convey positional information to other elephants, in order to aid navigation and congregation. So, for elephants this is more like a Harlem Shake that they use to indicate the site of their field party. In addition, elephant rumble vocalisations can also couple with the ground and propagate along the surface of the Earth. If in danger, elephants use all these signals as alarm calls to come together, as Dereck Joubert has observed that predators, such as lions, usually stay clear of large groups. Elephants appear to use bone conduction and specific mechano-receptors on their feet and trunk in order to detect these ground signals. This may explain why you sometimes see an elephant place the tip of his trunk on the floor or lean forward, putting more weight on his front feet.

So in fact body language spans from tiny flies to gigantic elephants. If these animals can communicate this way, surely many more species can too. Reginald Cocroft and Rafael Rodríguez estimated that at least 195,000 species of insects might use such body movements and vibrating signals to communicate. This is in addition to many species of arachnids, crustaceans, worms, frogs and vertebrates. It is therefore no wonder that we hold such a fascination for body shakes, which are clearly a basic and ancient mode of courtship and communication between animals. Would you really have thought that Earth is full of body shaking animals? I bet not. And we are only starting to discover the extent of it. So, in the meanwhile, do like so many in the world out there do, and 'shake your body down to the ground'!

Elephants 'shake the ground' and produce vibrations to communicate

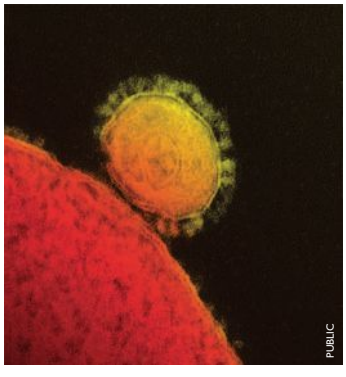
Caroline Fabre is an EMBO long-term postdoctoral fellow at DPAG Oxford and at the Department of Zoology

People do not have the monopoly on dancing in the animal kingdom


DANNI JERVIS

On the Origin of (a Virus) Species

Michael Nicoll investigates the recent outbreak of a new virus in the Middle East


PUBLIC

Transmission electron micrograph of Middle East respiratory syndrome (MERS) coronavirus

OUR USUAL BATTLES with viruses are mundane. After catching a cold we rest at home, tissues in hand, and wait for our immune system to squash the unwelcome bug. But what about other viruses out there? Dangerous strains of influenza, say, or perhaps an unknown enemy altogether? For unknown pathogens, worldwide surveillance for clusters of human or animal disease provides a way to sound the alarm before the bugs go viral.

In June 2012, Dr Ali Mohamed Zaki of the Virology Laboratory in Dr Soliman Fakeeh Hospital in Jeddah, Saudi Arabia, assessed a 60 year-old male patient admitted with pneumonia and acute renal failure. Taking a sputum sample from the patient, who would later go on to die of his infection, Dr Zaki was unable to identify the infectious agent with routine lab tests. He sent a sample to Dr Ron Fouchier in the Netherlands for further analysis. The diagnosis: a previously unidentified coronavirus.

We saw such an event in recent history. In 2003, the SARS coronavirus (SARS-CoV) hit headlines, sent face-mask sales soaring, vilified global air travel, infected roughly 8000 people and resulted in a case fatality rate of over 9 per cent. In the over 50s, nearly 50 per cent of infected people died. Now a new coronavirus had been uncovered– again the cause of a lethal pneumonia.

Further cases of the newly named Middle East respiratory syndrome coronavirus (MERS-CoV) occurred in Jordan, Saudi Arabia, Qatar and the United Arab Emirates (UAE), with infected air travelers carrying it further to Tunisia, Italy, France and the UK. With time it became no less devastating. As of early 2014, the total number of laboratory-confirmed cases was 184, as assessed by the World Health Organisation (WHO), with 80 being fatal.

To gain the potential to become pandemic–a global outbreak of the virus and its disease–MERS-CoV would require the ability to spread easily from person to person. Like related coronaviruses, transmission was assumed to occur efficiently through the air. But whilst early case reports describing MERS-CoV outbreaks within family groups and healthcare workers made for grim reading, it transpired that sustained close contact between individuals was necessary for the virus to spread.

Despite isolating infected individuals to limit the spread, recurring isolated outbreaks continued. With the world watching, scientists and medical professionals raced to identify the source of the new respiratory disease. With the majority of confirmed cases, the search focused upon the Kingdom of Saudi Arabia.

Where were people contracting the virus? To persist in the human population, continuous spread between people is a necessity. Was the severe disease the tip of a widespread 'MERS-iceberg'? Probably not–studies from 2013-14 found little evidence of MERS-CoV circulation in humans in either Jeddah or the Eastern Region within Saudi Arabia. So where was the virus coming from? And why was the outbreak limited to the Arabian Peninsula?

A clue came from the original virus isolated by Dr Zaki. Analysis of its genome determined that two bat coronaviruses, HKU4 and HKU5, were its closest relatives. SARS had also originated in bats infecting palm civets later sold in live animal markets in China, where human transmission could occur. Thoughts turned to the existence of an animal reservoir; an animal population in which the virus naturally


U.S. WILDLIFE AND FISHERIES SERVICE

Coronavirus infections are common in bats

circulated but from which it was now transmitting to humans. To date, research groups have indeed found highly related coronaviruses in Saudi Arabian and South African bats, with short stretches of MERS-CoV RNA detected in an individual bat near the site of the first human infection. Virologically speaking, bats are veritable zoos, and coronavirus infections are common. A 2013 *mBio* study determined that 58 different species from nine diverse virus families exist within just one bat species (*Pteropus giganteus*; the Indian flying fox). However, with bat-human contact rare, circumstantial evidence suggested another, unlikely, animal responsible for human infection: the dromedary camel.

When using the phrase 'animal reservoir', most imagine the animal kingdom spreading parasites and viruses via malarial mosquitoes, rabies-infected dogs, and Dustin Hoffman chasing a screeching ebolavirus-riddled capuchin monkey in the 1995 film, *Outbreak*. Not camels.

A 2013 report published in *Lancet Infectious Disease* suggested otherwise. When humans are infected with a virus, the immune system swings into action to clear the contagion. It also holds a grudge. Anti-viral cells and immune proteins called antibodies linger in our bloodstream, ready to pounce should a relative of the virus try to infect us again. The camel immune system is no different. Looking for these telltale signs of infection in retired racing camels from Oman and the Canary islands, researchers of the 2013 study found antibodies that bound to the MERS-CoV spike protein in 64 of the 155 animals tested, including all 50 from Oman. Furthermore, the antibodies did not react with a bovine coronavirus known to infect camels. Whilst no infectious virus or viral RNAs were isolated, making it impossible to determine whether they currently carried the virus, the camels had clearly been infected with a MERS-CoV-like virus.

Further evidence arose from the 11th known MERS-CoV fatality. A 43 year-old man was rushed to intensive care with pneumonia after spending days attending to a sick racing camel. Crucially, the Saudi Ministry of Health detected the presence of MERS-CoV RNA within the animal, confirming the presence of a MERS-CoV-like virus at the time of illness. The camel recovered. The owner did not.

However, despite evidence of camel and bat infection, there is no clear model for the transmission of MERS-CoV from infected animal hosts to humans. For many patients, animal contact was either not found or could not be determined. Is it possible that the trade in camel meat products in Saudi Arabia and the UAE may spread the virus through the food supply? It's a weighty claim, and whilst the WHO takes a cautious approach, stating that "sick animals should never be slaughtered for consumption", there isn't direct evidence to suggest this is a source of transmission. A 2013 report of simultaneous illness in goats and their MERS-CoV-positive Qatari caretaker may yet implicate more animals into the virus transmission cycle, but the fact is we still do not know how the majority of people become infected.

So, whilst continued surveillance and virus research are necessary to determine exactly how humans are contracting the virus, a final question begs answering: why are we only seeing human MERS-CoV infections now? Intriguingly, camels may have had the virus for over a decade. A report in *Emerging Infectious Diseases* posted online in January 2014 has shown that frozen camel serum samples from 2003 also test positive for MERS-CoV antibodies–nine years before human infections were first recorded. Have human infections occurred before but gone unnoticed–simply recorded as pneumonia without a second thought? Or has the virus mutated in its natural host (or hosts) and gained the ability to transmit to humans for the first time? And, if so, will human infections become ever more common? Unfortunately, as with much of MERS-CoV's mysteries, we are going to have to wait and remain vigilant to find out.

In the meantime, keep a suspicious eye on the camels, and watch out for their spit.

Antibodies against MERS-CoV, or a related coronavirus, have been found in camel sera

Keep a suspicious eye on the camel's spit!

Michael Nicoll is a post-doctoral researcher at the Department of Pathology

Health-boosting Greens?

Ricardo Milho examines the evidence behind the 'superfood' claims of cruciferous vegetables

'Superfoods', including cabbage, kale and cauliflower, are high in isothiocyanates

IT IS AN ACCEPTED wisdom that a diet rich in vegetables is good for us. Many chemicals present in plants, such as those responsible for their colour, smell and flavour have been shown to be beneficial for our health. Examples include lycopene in tomatoes, *B*-carotene in carrots, resveratrol in the skin of red grapes and the antioxidant catechin in green tea. Many of these compounds cannot be synthesised by humans and therefore have to be sourced from our food intake. Some of these micronutrients, such as vitamins, have long been recognised to play a vital role in our health. But many other compounds, not yet considered essential, are likely to be beneficial. These are commonly referred to as phytochemicals.

Scientists have identified thousands of phytochemicals, but few have been studied closely. Due to the complexity of the biochemical processes in which these compounds are involved, it has been difficult for researchers to find out which phytochemicals may help fight specific diseases, which have no effect and which may be harmful. Despite these uncertainties, the Western world has become increasingly fascinated by the purported health-promoting properties of so-called 'superfoods'. Is the term 'superfood' a mere marketing tool? Although scientists often dispute the alleged health benefits of certain foodstuffs, sales of products like blueberries have soared in recent years. To protect consumers from misleading marketing claims, in 2007 the European Union banned the use of the term 'superfood' in food packaging unless accompanied by credible scientific research. However, emerging evidence about two different groups of phytochemicals found in dark green vegetables may justify the inclusion of these plants in the 'superfood' category.

Most dark green vegetables consumed by humans belong to the family *Brassicaceae*, also known as cruciferous vegetables due to the characteristic shape of their flowers. The four petals resemble a cross (*Cruciferae*, Latin for cross-bearing). This family includes widely cultivated vegetables such as broccoli, Brussels sprouts, cabbage, cauliflower, kale, turnip and watercress. Scientific interest in crucifers has increased with the finding that isothiocyanates and indole-3-carbinol, unique phytochemicals present at high levels in these plants, have the potential to prevent a wide range of cancers and multiple inflammatory disorders.

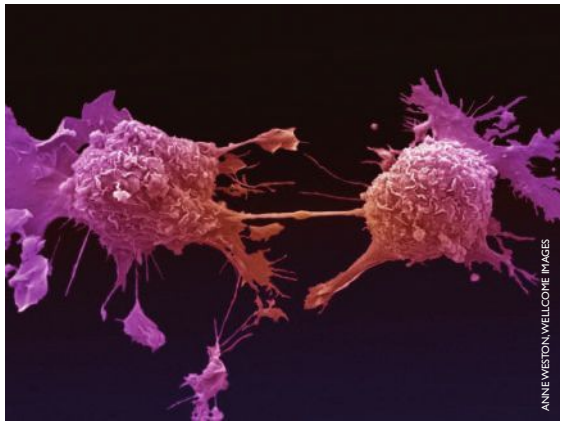
Cruciferous vegetables get their name from the petals of their flowers, which resemble a cross

The pungent taste of some cruciferous vegetables, such as Brussels sprouts, is due to the presence of isothiocyanates. Natural isothiocyanates are produced by specialised cells in these plants upon tissue damage as a defence mechanism against herbivores and pathogens. The potential benefits of these compounds for human health were first shown by studies performed on rodents during the 1960s and 1970s. In a seminal publication in 1977, Wattenberg found that they reduce the impact of exposure to cancer-inducing chemicals. In the following year, an epidemiological study in humans found that individuals who consume fewer cruciferous vegetables have an increased risk of developing colon cancer. Finally, a third study showed that isotiocyanates prevent rodent models who had been genetically predisposed to cancer from developing tumours. Furthermore, this protection

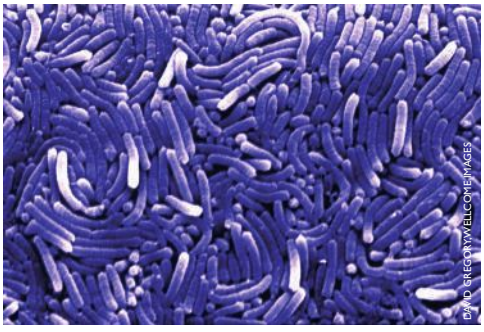
is not organ-specific and has been observed in the lung, oesophagus, stomach, colon, mammary gland, bladder, pancreas and skin.

Attempts to understand the mechanism of action of isothiocyanates began in parallel with studies demonstrating their protective effect in animals. It is now clear that there are multiple mechanisms, including stimulation of toxin-metabolising enzymes, induction of apoptosis (the process of programmed cell death), and antioxidant and anti-inflammatory activities. Multiple clinical studies have shown that the stimulation of toxin-metabolising enzymes by isothiocyanates ultimately lowers the levels of dangerous substances capable of mutating DNA, thus helping to lower the occurrence of cancerous cells. This detoxification process is particularly relevant in the protection against environmental pollutants. In the advent of cancer, the ability of isothiocyanates to induce apoptosis helps to reduce tumour growth. However, the benefits of these phytochemicals do not apply exclusively to cancer. Oxidative stress and chronic inflammation can lead to the development of multiple diseases. Indeed, the protective effects of isothiocyanates have been demonstrated in rodent models of cardiovascular and kidney diseases in models of nervous tissue injury and neurodegeneration, and in restoration of skin integrity. These compounds also help humans infected with *Helicobacter pylori* to reduce stomach colonisation by this bacterium, which is strongly associated with the development of gastric cancer.

There is now a wealth of evidence regarding the health benefits of isothiocyanates. Unlike most pharmacological agents that usually affect single targets, isothiocyanates have multiple targets. It is this ability to induce versatile and long-lasting responses that makes these unique phytochemicals exceptional protective agents. While isothiocyanates help to protect against the onset of disease, other phytochemicals present in cruciferous vegetables may contribute directly to maintaining the normal function of the human body. An example would be indole-3-carbinol, as demonstrated by the work of Marc Veldhoen and his team at the Babraham Institute, in Cambridge.


ANNE WESTON, WELLCOME IMAGES

The surfaces of our body organs, especially the intestines, are colonised with a large variety of bacteria. Although many are beneficial, the intestine still needs protection against excessive epithelial invasion by these and other microorganisms. Underneath the layer of epithelial cells that form the internal surface of the intestine, there is a network of specialised immune cells. These cells, called intraepithelial lymphocytes, play a fundamental role in protecting the intestine against infection and excessive inflammation. Intraepithelial lymphocytes express high levels of a specific receptor: the aryl hydrocarbon receptor (AhR). It was known that AhR signalling is required for the normal function of these cells but until recently the molecules recognised by AhR were unknown.


DAVID GREGORY, WELLCOME IMAGES

Isothiocyanates can reduce stomach colonisation by *Helicobacter pylori*

Through a series of experiments performed on mice, Veldhoen and his team showed that the molecules that bind AhR, derive predominantly from dietary phytochemicals. The researchers manipulated the diets of mice, switching them to a synthetic feed lacking ingredients of vegetable origin. The altered diet led to a decrease in the numbers of intraepithelial lymphocytes in the intestines, which enhanced susceptibility to damage and increased numbers of harmful bacteria. However, when the diet was supplemented with indole-3-carbinol, these alterations were essentially reversed. Thus, the team concluded that plant-derived dietary compounds, such as indole-3-carbinol, promote normal immune function in the intestine.

The studies described here significantly expand our understanding of how diet impacts our well-being, showing that plant-derived nutrients can shape our capacity to fight disease. Nonetheless, some questions remain unanswered. For example, in comparison with human dietary exposures, many animal studies use relatively high doses of isolated phytochemicals. So it is not yet possible to recommend a particular 'human dose'. Clinical trials are underway to evaluate the toxicity and potential side-effects of these isolated compounds in humans. Nevertheless, if you were reluctant to introduce cruciferous vegetables into your diet, these thoughts should provide you with enough encouragement to eat your greens. These 'super' veggies may help you fight off chronic diseases and keep your intestines healthy!

Consumption of cruciferous vegetables can prevent cancerous tumours forming in many different tissues including lung, stomach and colon

Ricardo Milho is a post-doctoral researcher at the Department of Pathology

Decision-making and co

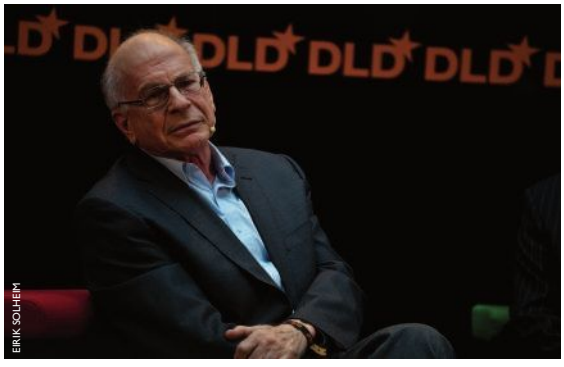
ognitive biases

BlueSci explores biases in human cognition, from their evolutionary background to their socio-political implications

HUMANS, AND ORGANISMS IN GENERAL, are faced with different possibilities and trade-offs in every aspect of their lives. When to reproduce or divide? When to fight or flee? Which political party to elect? Rationality is held by many people as intrinsic to human behaviour. We assume that rational decision-making underlies our cognition, and that we make decisions by finely weighing options and thoughtfully calculating outcomes. However, decision-making processes in human and non-human animals are pervaded with biases. In this article we discuss some of the most striking cognitive biases known in human decision-making, focusing on the economic, social and political implications that they can have. We then contrast these processes with less-biased decision-making programs in computers, and close the article by discussing the potential evolutionary explanations behind cognitive biases: why are they there?

According to economists, if humans are 'rational' and free to make choices then they should behave according to the 'Rational Choice Theory' (RCT), which states that people should make decisions by determining the value of a potential outcome, how likely this outcome is, and multiplying these factors. Daniel Kahneman and Amos Tversky were two of the first social psychologists to empirically prove that this is frequently not the case, and that decision-making processes have many biases. After their first work in the 1970s, the list of known cognitive biases has increased greatly, and their work set out a paradigm in psychology and economics of humans as irrational decision-making agents.

Let's start by describing a bias in an everyday situation. We may think that the opinion we have of somebody depends on a deep scrutiny of what we know about them, but in reality this is not the case. We tend to have limited information about people, and we extrapolate this information to other aspects of their personality or abilities. This phenomenon, known as the 'halo effect', was first described by Edward Thorndike in 1920 after he

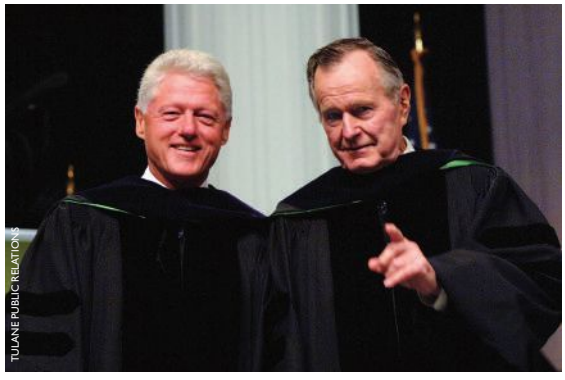


Daniel Kahneman was one of the first social psychologists to experimentally show cognitive biases

asked commanding officers to evaluate their soldiers according to the physical qualities and intellectual capabilities they possessed. He found that whenever a soldier scored well in one category, he would rank well in all categories. Basically we assume that because someone is good in task A, then he or she will also be good in task B. The halo effect has been studied in different scenarios with remarkable results being found. For instance, students have been shown to rank essays as better written if they think the author is attractive than if they perceive the author as unattractive. Another study carried out in 1975 found a correlation between the attractiveness of criminals and the harshness of the sentence they would receive: the more attractive the criminal, the less likely they were to be convicted, or the lighter the sentence that they would receive.

Political campaigns too can be influenced by the halo effect. A study carried out by Melissa Surawski and Elizabeth Ossoff in 2006 confirmed this by asking participants to rate the political skills of candidates after showing them photographs and playing audio clips of them. They found that physical appearance predicted the candidate's competency better than voice. A recent study on US congressional elections also showed that winning was strongly affected by inferences of abilities based on facial appearance.

Another cognitive bias that can have profound socio-political implications is the 'bandwagon effect', where individuals support the opinion of the majority of their peers. This effect is particularly relevant in politics, where voters may alter their decision to match the majority view and hence be on the winner's side. For example, in the 1992 US presidential election, Vicki Morwitz and Carol Pluzinski conducted a study in which they exposed a group of voters to national poll results indicating that Bill Clinton was in the lead, while keeping another group unaware. They found that a number of voters in the former group who intended to vote for George W. Bush changed their preference after seeing these results, while the latter group didn't change their decision. Studies have also looked at a counter-acting bias known as the 'underdog preference', a rarer phenomenon than the bandwagon effect, wherein some people may support the less-favoured candidate or sports team in a match to feel fair.



The 'bandwagon effect' was tested during the 1992 US presidential election

How about when we have to decide between two options? If we were to make a rational decision when comparing two alternative options then the relative proportion of choices made between them should be the same regardless of whether they are presented to us on their own, or whether a less-preferred, third option is presented alongside. Nevertheless, this less-preferred third option can make us change our opinion about the other two, better options. This is the 'decoy effect', and it happens when a preference between two options changes when shown a third option that is asymmetrically-dominated, meaning it is inferior in some way and superior in another to one option but inferior in all aspects to the other option. To illustrate this, imagine trying to decide between two train tickets to London, which vary in price and duration of the journey:

	Ticket A	Ticket B
Price	£40	£30
Time	30 min	40 min

It may be difficult to decide between these two, and some people may decide for ticket A and some for ticket B depending on their priorities. But what would happen if we included a third option that was more expensive than both A and B, but took longer than A?

	Ticket A	Ticket B	Ticket C
Price	£40	£30	£45
Time	30 min	40 min	35 min

In this case, the asymmetrical decoy (Ticket C), would make option A more appealing than option B.

Interestingly, the decoy effect has also been described in non-human animals. For instance, Melissa Bateman and her colleagues studied the foraging behaviour of hummingbirds by placing birds in two different scenarios. In one scenario the birds had to choose between two alternative artificial flowers, and in the other scenario they had to choose between the same two flowers and an asymmetrical decoy:

Artificial flowers	Scenario A		Scenario B	
	Quantity	Conc	Quantity	Conc
Target	15 µl	40%	15 µl	40%
Competitor	45 µl	30%	45 µl	30%
Asymmetric decoy	Not present		10 µl	35%

The target flower offered less food but a higher sucrose concentration than the competitor. The asymmetrical decoy in scenario B was worse than the target in both aspects and better than the competitor in terms of sucrose concentration, but not in the total amount of food that it provided. Birds that were exposed to the decoy option showed a higher preference for the target flower than birds that did not have access to the decoy.


ALANA SISE

Hummingbirds, like humans, are influenced by the 'decoy effect'

The decoy effect has been studied in many different circumstances with remarkable effects being found. For instance, Joel Huber, a marketing professor at Duke University, showed how it can affect our preference for restaurants. He asked people if they would prefer to have dinner in a five-star restaurant that was farther away or in a closer three-star restaurant. With these alternatives some people would prefer the five-star restaurant and some the three-star restaurant. But once he included a third option, a four-star restaurant that was farther away than the first two restaurants, then more people preferred the five-star restaurant over the three-star one.


STEVE LOYA

The 'decoy effect' can sway our choice of food or restaurants

A well-known scenario where biases blur our choice is when we are confronted with risky decisions. Let's imagine that flooding in a city prompted the council to announce two emergency schemes to limit the damage from the flooding: we could either pile up sandbags everywhere, which would save about a quarter of the city from flooding, or we could invest in an experimental and risky flood barrier, which has a twenty five per cent chance of saving the entire city and a seventy five per cent chance of failing and saving nothing. Which solution would you choose? Now imagine that an updated risk assessment comes in about these two solutions. It turns out that piling up sandbags is actually going to cause three quarters of the city to be flooded, while the flood barrier has a seventy five per cent chance of causing the whole city to be flooded, and a twenty five per cent chance of preventing the flooding completely. Which solution would you choose this time?

Most people would have chosen the sandbags the first time, and the flood barrier the second. But as some of you may have noticed, the options were identical in both cases. All that changed was the framing: describing the positive effects of the measures the first time, and the negative effects the second. This 'framing effect' is related to our instinctive loss aversion. We hate losing out on something we already have, and will take riskier decisions (the uncertain flood barrier) to try and maintain it. On the other hand, when it comes to gains, we prefer a decision with a certain and reliable outcome (the sand bags). This causes our behaviour to change, in identical circumstances, depending on whether an outcome is presented as a potential loss or a potential gain. These are just some examples of dozens of known, named and heavily researched systematic biases that exist in human decision-making. But is there a way of making un-biased decisions?

Thanks to the work of Kahneman and Tversky, computer-based decision-making has come to replace human decision-making in many walks of life, reducing the biases in some choices. Think of Moneyball, the story of the team that

Oakland Athletics used an evidence-based approach to select players

revolutionized baseball by ditching the tips of talent spotters in favour of statistical analysis in order to buy undervalued players and turn their prospects around. These techniques, once employed only by statistically-gifted mavericks, have become commonplace in courtrooms and hospitals, where a failure to recognise biases can have drastic consequences. A popular way of getting computers to do this relies on a branch of maths called 'Bayesian inference'.

Generally, theories can predict how experiments should work, but real data is often messy and experiments frequently go wrong. Scientists need to work backwards from the experiments to decide which theories are best, and to modify these theories to fit better with the observed results. The mathematical principle behind how scientists do this is termed Bayesian inference: what should we believe, and how confident of it should we be, given the data? It's basically a method of updating probabilities when new information is acquired. Bayesian inference requires 'priors', or information of how likely a theory is before starting an experiment. Priors used in Bayesian inference can be based on previous experience or general knowledge of the world. Not expecting a particular result more than any other can be the best choice in some cases.

A common human bias is that of ignoring 'statistical priors' when evaluating new information. For instance, in one of Kahneman and Tversky's experiments they gave subjects descriptions of several people's personalities, and asked them to guess if they were engineers or lawyers. The descriptions gave no occupation-specific information, but one group of subjects were told that the people came from a population with seventy per cent lawyers and thirty per cent engineers. The other group were told that the percentages were reversed. Bayesian inference states that if there are more engineers present, we should guess that more of the people described are engineers. However, in the experiment the two groups entirely ignored the information on the population as a whole and gave the same responses, no matter how vague the description was. Only if no personality description was given did the two groups give predictions that resembled the population divide.

Bayesian theory is often used as the basis of machine-learning, where computers predict or discover things about the world from large data-sets. For instance, naïve Bayesian classifiers are used to infer whether people who have been arrested are likely to commit crimes again if released on bail. To do this, first a program is trained with existing data on people previously released on bail, and information on whether or not they committed crimes before the trial was over. The program then establishes relationships between certain variables, or risk-factors, such as criminal records, social and economic situation, and reoffending rates. Afterwards the program can be used to predict the outcome of releasing criminals, with the first set of learnt relationships used as priors. When comparing the output of the program with decisions made by judges, it transpired that judges' subjective decisions had been completely misguided. Between their personal biases, and the fact that some people could not afford to post bail, the judges effectively released people at higher risk of re-offending while on bail.

The outstanding prevalence of biases in decision-making processes begs the question of why we, and

Computer-based decision-making programs are used in courtrooms to decide whom to release on bail

animals in general, have these biases to begin with? Could there be an advantage to them or are they just an evolutionary solution to compensate for our limited cognitive ability?

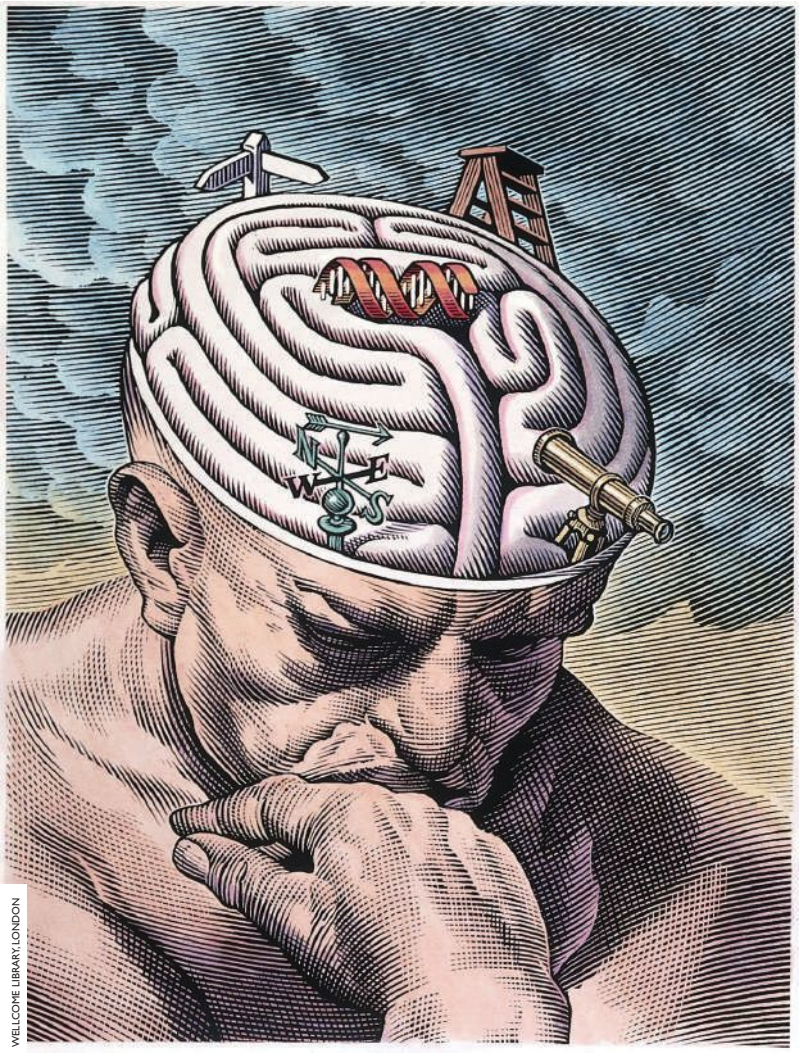
Every individual, from the smallest virus to the largest whale, faces trade-offs during its lifetime. Resources are limited, and individuals are selected to maximise their lifetime reproductive success: getting the highest benefits with the lowest costs, according to the resources available. This is the basic principle of natural selection, the main driving force of evolution. Cognition is no exception. Our brain has been moulded by natural selection throughout our evolutionary history to adapt to the environment under which it evolved. Under this perspective the mind is 'adaptively rational', comprising a set of tools designed by natural section to deal with situations our ancestors encountered. This concept has led to the idea of 'ecological rationality', which suggests that cognitive biases are a result of adaptive solutions to

the decision-making problems of our evolutionary past, that maximised the ratio between the benefits and costs of decision-making.

Two of the strongest arguments linked to ecological rationality are 'heuristics' and 'error management'. Heuristics are efficient solutions to problems when information, time, or processing capabilities are constrained, while error management suggests that natural selection favours biases towards the least-costly error. An experiment that illustrates the idea behind heuristics was done by Andreas Wilke in 2006; he studied the foraging behaviour of people–when they would decide to leave their current resource patch and move onto a new patch–under different resource-distribution situations: random, evenly-aggregated or evenly-dispersed. He found that humans used the same set of rules to change resource patches independently of the distribution of food, always using rules that were particularly useful for aggregated resources. Although this result seems irrational, if we consider how resources are distributed in nature it becomes less puzzling; aggregated patches are more common in nature because species are not independent of one another–they tend to attract or repel each other. Using a straightforward rule that is useful in most patches can be a more efficient solution than carefully calculating the amount of food in each patch and deciding when to leave afterwards.

The idea of error management comes from the theory that eliminating all possible errors when making decisions may be impossible, so there may be selection to reduce the most-costly errors. For instance, being able to identify poisonous animals like snakes requires observation and identification of the object. There are two possible outcomes to this: a person could properly examine a potential threat and correctly classifying it as a snake, or could walk away without the certainty that it was in fact a snake. Either way, an error is likely to occur, so it may be more advantageous to have a bias that makes people run away from things that resemble snakes, even if sometimes they run away from lifeless objects, than to get close to the object to decide if it is actually a snake or not. In this second case, the likelihood of being bitten will be larger, as is the cost of the error. Error management may increase the overall rate of making errors, but minimises the overall costs of the errors made.

Ecological rationality leaves us with two ideas. One is that our brain has an optimal design that maximised the benefit-to-cost ratio of cognition during our evolutionary history. An optimal design need not necessarily be a 'perfect design', since the costs associated with producing and maintaining it could be too high, but another hypothesis that emerges is that, under some circumstances, biases could have a selective advantage. Whatever the reason behind our cognitive biases, one thing is certain: the study of how our brain works and how it evolved is a topic that has brought together the minds of economists, psychologists, philosophers, physicists, engineers, neuroscientists, medics, mathematicians and biologists. It is perhaps one of the most interdisciplinary lines of research, and one of the most interesting mysteries of our time.



Studying the inner- workings of the mind is one of the most interdisciplinary fields of research

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Decoding Quantum Computing

Simon Watson demystifies the complex world of quantum computing

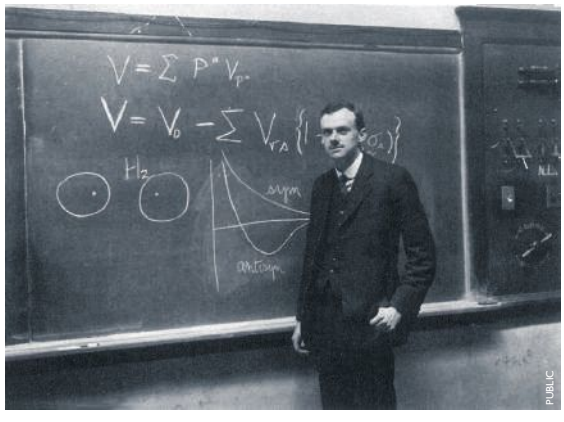
Paul Dirac introduced the principle of quantum superposition

QUANTUM COMPUTERS ARE regularly heralded as the future of computing, harnessing the power of atoms and elementary particles to perform calculations that today's computers could only dream of. Quite how this remarkable feat is achieved is either complicated with jargon such as 'qubits', 'superposition' and 'entanglement' with no further description, or dismissed as too complicated for a layman. This article aims to explain how quantum computers work, why they're faster than classical computers, and why they're not a replacement for them.

Before we can describe how a quantum computer works, we need to understand today's classical computers. Currently, computers work by manipulating 'bits' of data. A bit is something that can take one of two values, commonly written as 0 or 1. For example, a coin can be either heads or tails, or a light-switch can be on or off. In the case of a computer, the values may be a charged or discharged capacitor in memory, or the presence or absence of a groove on a CD. Computers operate on strings of eight bits, termed a 'byte'. These bytes form instructions sent to the computer's processor, directing it to perform functions such as adding two numbers, printing to the screen, or writing to memory.

CDs store information through the presence or absence of grooves

Quantum computers work fundamentally differently. Rather than using a difference in electric voltage to encode the bit values, they use the physical properties of fundamental particles or atoms. As long as there are two different measurable states, a bit value can be stored. For example, electrons are sub-atomic particles that have a property called spin. This can be imagined similar to the rotation of a ball around its axis; just as a ball can rotate clockwise or anti-clockwise, electrons can have a spin value of 1/2 or -1/2 (termed 'up' and 'down'). The bit value can therefore be assigned by measuring the spin state of the electron. Another example would be the polarization state of light. Light travels through space as a transverse wave, oscillating perpendicular to its direction of motion. A wave travelling along for example the z-axis can be oscillating about either the x- or y-axis. We could therefore store the bit value by whether the light is horizontally- or vertically-linearly polarized.

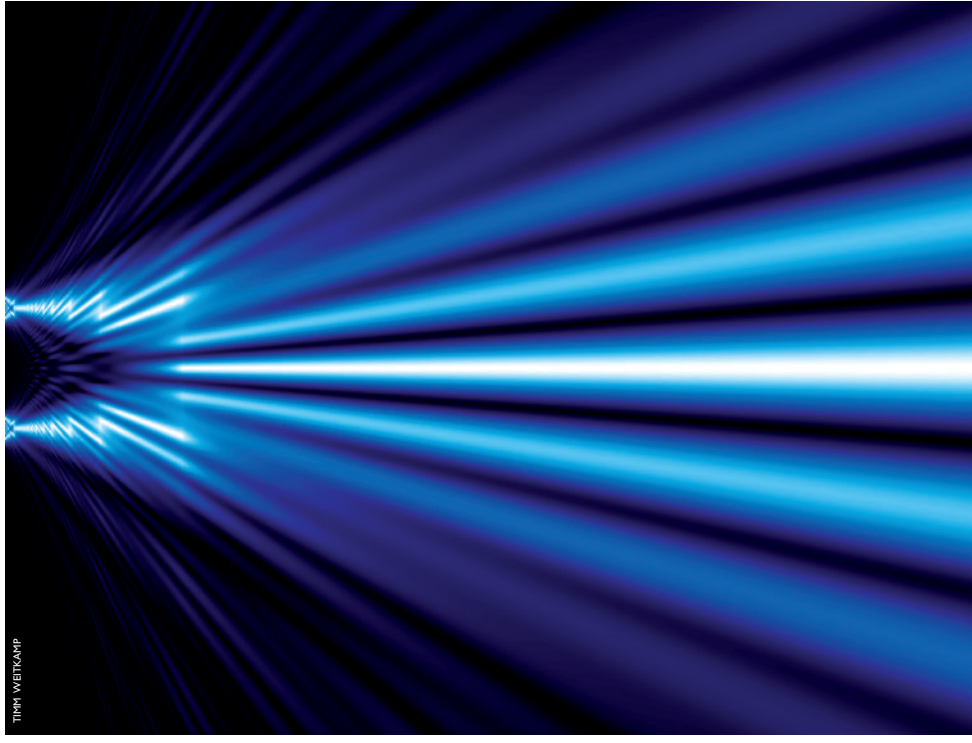


Were the analogy to end there, quantum computing would be no more complicated than classical computing. However, in 1930 theoretical physicist Paul Dirac published the first edition of his book *The Principles of Quantum Mechanics*. In it, he introduced the world to the revolutionary concept of 'quantum superposition' that now forms the backbone of quantum mechanics. Dirac was trying to explain the baffling evidence that light acts as both a wave and a particle–the so-called 'wave-particle duality' theory. On the one hand, Thomas Young's double-slit experiment showed that when a laser was shone through two parallel slits, it diffracted like a classical wave, with the two waves interfering with each other where they were out-of-phase. In contrast, alternative evidence, such as the emission of photoelectrons by atoms when they absorb light of a particular frequency, showed that light was composed of discrete particles with definite energy and momentum, termed photons. Dirac considered the problem of a beam of light containing a single photon passing through a double-slit. For the light to pass through the apparatus and cause an interfering diffraction pattern the single photon must partly go through both slits, with each part interacting with the other–it is in superposition! This idea of wave-particle duality and superposition was later shown to not be restricted to light, but universally extended to all particles. Quantum superposition therefore holds that a physical system exists at some probability in all possible states simultaneously.

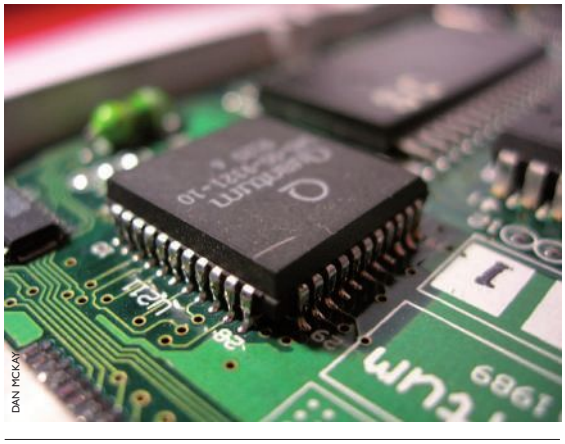
This phenomenon of superposition becomes even more bizarre when you extend it to particles that originate from the same source or are brought to interact together. Such particles do not exist in superposition independent of each other, but rather their quantum states become 'entangled' so that their physical properties can only be described relative to each other. For example, a particle with spin 0 may decay into two particles, each with spin 1/2. These particles, because they are entangled, exist in superposition where in addition to both being spin up or down at some probability, they have a probability of being in their anti-correlated spin states up/down and down/up simultaneously. They therefore do not individually have a spin direction of their own, but rather their state is defined as being opposite each other.

If we return now to the quantum computer, quantum mechanics dictates that in addition to the quantum bit (termed a 'qubit') having two measurable states (for example, spin up or down), it exists in a superposition where it has both states at the same time. It therefore has some probability of being both 0 and 1 at the same time. This means that the amount of information each qubit can hold is significantly larger than its equivalent bit. Consider a computer consisting of two classical bits. To fully describe the possible states of the system (00, 01, 10, 11), only the values of each bit are required. So the computer has an information capacity of two. The corresponding quantum computer has its entangled qubits in a superposition of all states, with a separate probability of being in each state: the probability of being in state $|00\rangle$ (for example, both electrons have spin down) is a; the probability of them being in state $|11\rangle$ (for example both electrons have spin up) is b; and the probability of being in states $|01+10\rangle$ and $|01-10\rangle$ (that is in an entangled superposition) is c and d respectively. To fully describe this quantum system, four probability values (a, b, c, d) are required. This two-qubit system therefore holds double the amount of information as the classical two-bit system, with each additional qubit exponentially increasing the amount of information it can contain. A system with 10 qubits holds the same information as 1024 classical bits, while 300 qubits holds more information than there are particles in the universe!

However, accessing the information stored in these qubits is not a simple matter, as superposition doesn't automatically make any computation faster than a classical computer. The quantum computer must be designed, and quantum algorithms written specially, to utilise the probabilities in the entangled qubits' superimposed states and get the desired speedup. Otherwise it is nothing more than a very fancy, but expensive, classical computer containing only a few bits. This severely constrains its applicability to solving specific problems, such as using Shor's quantum algorithm for factorising integers. While this doesn't sound very exciting, the widely-used public-key cryptography relies on the intractable time it takes to factorize very large numbers in keeping messages encrypted. If quantum computers can factorise quickly, these encrypted messages can be easily read. However, to date the largest integer that has been successfully factorised by a quantum computer is 143! Much money and research is therefore being invested in this field; in 2013 Canadian company D-Wave claimed to have a 512-qubit computer that solved a Travelling Salesman problem over 3,600 times faster than a classical computer. So, while quantum computers will probably not replace personal computers, they are also not just a proof of concept.



Thomas Young's double-slit experiment showed that light behaved as a wave



Canadian company D-Wave are making the concept of quantum computers a reality

Simon Watson is a postdoctoral researcher at the Wellcome Trust Sanger Institute

The Psychology of Discrimination

Alex O'Bryan Tear discusses the psychology behind racism

Nelson Mandela believed nobody was born racist

"**NO ONE IS BORN** hating another person because of the colour of his skin, or his background or religion. People learn to hate, and if they can learn to hate, they can be taught to love, for love comes more naturally to the human heart than its opposite." These words capture Nelson Mandela's message to the world.

However, developmental psychologists have shown that new-born babies are in fact racist. Neonates, despite their near-blindness, are rapidly able to distinguish between ethnicities by both sight and sound, showing signs of fear and distrust towards ethnicities different from those of their caregivers. There is similar evidence for discrimination on the basis of religion, gender and socio-economic background as soon as these categories are identified by the maturing child. Apparently, this tendency need not be taught. And though it might be overwritten through education, the residue can be shown to linger, unvoiced, in nearly everyone.

5-7 year-old children show racist tendencies when answering questionnaires

One common approach to teaching children tolerance is to try and avoid drawing attention to differences between societal groups. However, it seems that children seek out these distinctions, using them to form divisions and ultimately prejudices. Brigitte Vittrup gave 5-7 year old white children a questionnaire of the form "What proportion of [white/black] people are [positive/negative adjective]?" The children, in their innocence, were more than willing to assign a higher proportion of black people the negative adjectives and a higher proportion of white people to the positive ones. Vittrup concluded that this apparent open racism was due, in part, to the parents' well-meaning attempt to be 'colour-blind' by not discussing race openly. Perhaps they hope, like Mandela, that quashing racist ideas is simply a case of not teaching them.

A few years later, very few children are openly racist. But have these children learned to be genuinely accepting, or have they simply discovered that racism is not socially acceptable? This same question can be asked of adults, of course, and to answer it we turn to a more subtle measure: the Implicit Association Test (IAT), developed by Anthony Greenwald. The IAT uses a basic psychological measure–reaction time–to reveal attitudes that people may be unwilling to express openly. In the simplest version of the experiment, the participant is asked to make one of two categorization tasks. Either a name appears on the screen, for example 'Nelson Mandela', which must be categorized as either 'white' or 'black', or an adjective appears on the screen, for example 'happiness', which must be categorized as either 'pleasant' or 'unpleasant'. The rub comes in the fact that the same set of two keys is used to make these categorizations. In one testing block, the participant uses one key to make the 'black' or 'unpleasant' choice, and another to make the 'white' or 'pleasant' choice. In the other, these pairings are reversed: one response means either 'black' or 'pleasant', while the other means either 'white' or 'unpleasant'. White participants, to varying degrees, respond more slowly in the latter testing block than in the former, implying that the association between 'black' and 'pleasant', or between 'white' and 'unpleasant', is harder to make than the association between 'black' and 'unpleasant', or 'white' and 'pleasant'.

This experiment has been refined and extended in a number of ways: to other races, other group divisions such as sex or status, or to other associations, such as more specific stereotypical ideas. In all cases, the results paint a gloomy picture of our innermost, implicitly held attitudes. Many studies, as well as the IAT, point to the same conclusion. Despite the veneer of socially acceptable egalitarianism, it seems Avenue Q had it right: "everyone's a little bit racist".

To understand these alarming findings, we turn to Henri Tajfel and John Turner's 'social identity theory'. Tajfel and Turner claim that we instinctively divide everyone into two groups: the in-group and the out-group. The in-group is populated with 'people like us': friends, family and anyone who we want to be associated with. These are the people to whom we naturally extend trust and affection, and are more likely to pay favours. The out-group is populated with everyone that didn't make the cut. Our instinct is to distrust them, avoiding them as much as possible. When this tendency goes

unchecked, we begin to homogenise them, building up a stereotypical list of skills, attributes and attitudes. We selectively remember and exaggerate positive information about the in-group, while doing the same for negative information about the out-group.

Perhaps surprisingly, discrimination isn't reserved for the broad and salient categories of sex, status or race. It operates at a hair trigger, sorting people along any dimension. Tajfel developed the idea of the 'minimal group' to demonstrate just how easily social identities can arise. He asked participants to select which of two pieces of abstract art was their favourite, and established two groups on this basis. He found the same differences in treatment emerged, even using this apparently meaningless distinction, between the in-group and the out-group. Members of one group were more likely to stereotype members of the other group, and ascribed more positive traits to members of their own. When given a choice between ways to divide cash prizes, they favoured members of their own group, and sought to maximize the difference in the prizes received between their group and the other–even if this meant accepting a smaller prize themselves.

Anthropologists and evolutionary psychologists have a ready explanation for this ingrained behaviour. They argue that it is ultimately because our social skills evolved in environments with closely-knit tribal communities, numbering no more than about 150 people. Members of other tribes were, at best, competitors for resources and, at worst, hostile enemies. A premium was placed on rapidly distinguishing between friend and foe, and on clearly demonstrating one's own tribal allegiance. This remained even as societies evolved into larger units. Nationalism and religious allegiance allowed societies full of strangers to develop mutual trust through a sense of shared identity, which had a flipside: a common sense of distrust, directed at the similarly larger out-groups. Today, as Seth Godin and many others have pointed out, we see our tribal mentality resurfacing everywhere from the workspace, to the football club and the blogosphere, carving out groups from the mass of people we encounter, and protecting us by labelling everyone we meet as friend or foe.


SE KWIEN

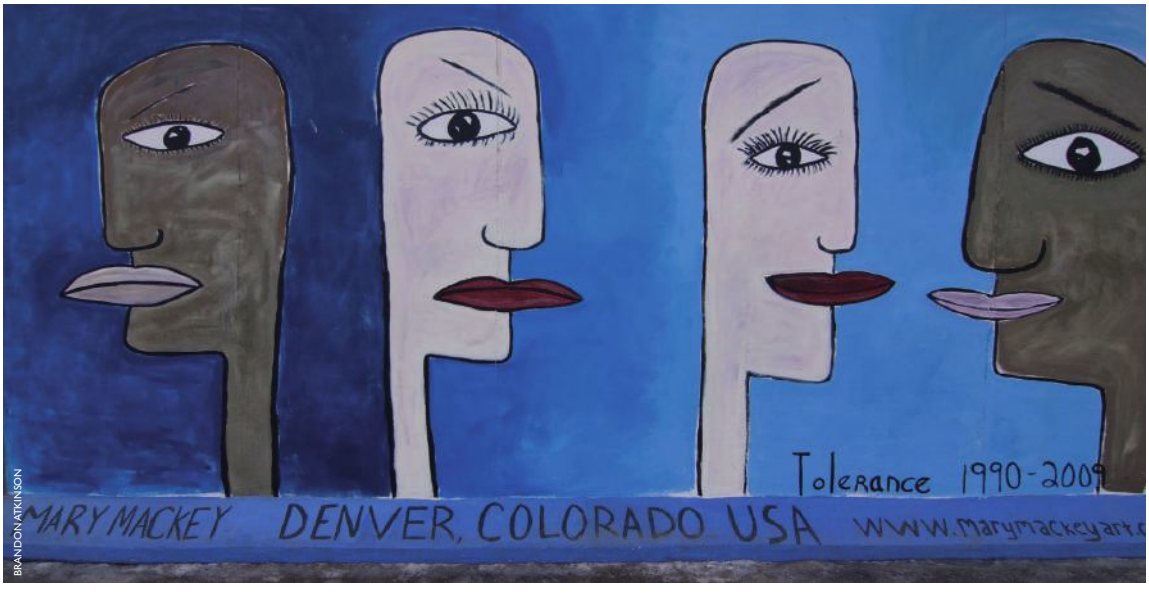
Mandela donned a Springboks rugby jersey to offer people a new 'in-group'

It seems as though our tendency towards group discrimination is here to stay. Although we struggle to supress it, the good news is that it's flexible enough to be harnessed for good. Mandela demonstrated a vital tool that is being used today to promote harmony in the ghettos of Detroit. By donning a Spingboks jersey, he offered the people of South Africa a new in-group which cut across the boundary of race. Rejecting old group divisions in favour of new and inclusive ones harnesses our innate group mentality for positive ends.

With the historical progression of society into ever-larger units we can already see a corresponding expansion of the in-group. Group mentality now operates at the global level. Early anti-apartheid action failed, arguably, because it emphasised black rights. It entrenched the group divide, making it impossible for either white or black South Africans to forget their own sense of allegiance. Mandela, and every great civil-rights activist, succeeded by instead emphasising the traits that transcend all global categories, uniting South Africans in their shared humanity. In this way, Mandela created a new in-group, to which everyone belonged.

So, Mandela was at least partly right. We can be taught to love. However, this fraternal love has a dark side: a natural tendency to discriminate between insiders and outsiders. It's only by coming to terms with our innate psychological foibles that we can mobilise them for good.

Alex O'Bryan Tear is a 2nd year PhD student at the Department of Psychiatry



BRANDON ATKINSON

It's only by coming to terms with our innate psychological foibles that we can mobilise them for good

Royal to the Bone

Charlotte Houldcroft outlines the scientific techniques used to identify dead royalty

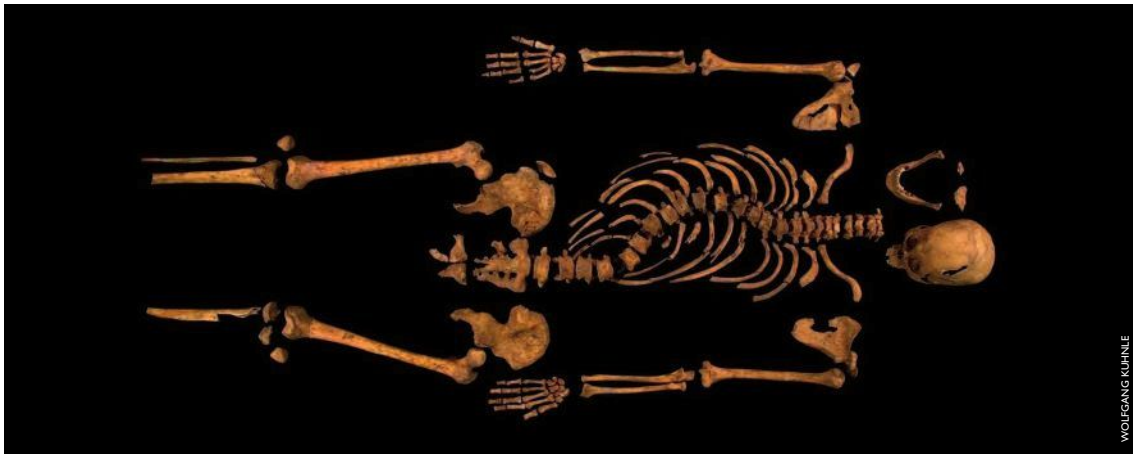
Prince Phillip's mitochondrial DNA was used to identify remains of the Romanovs

Europe's relationship with royalty has often been a troubled one. When warring dynasties weren't battling to replace one another, oppressed members of the populace were plotting revolutions, or fanatics made assassination attempts. Later, rulers deliberately or accidently decimated the last resting places of their forebears, leading to the loss of the bodies of kings and queens. However, there has been a recent trend to excavate and identify the remains of these lost royals across Europe. The skeleton of Richard III was discovered recently in a car park in Leicester, but the remains of the Romanovs, the last Tsars of Russia, and the embalmed head of Henri IV of France have also been unearthed. Archaeologists from the University of Winchester are hoping to give Alfred the Great the same treatment. A variety of scientific techniques drawn from forensics, archaeology, genetics, cancer-care and chemistry are helping to give names, and a royal reburial, to bones long thought lost.

The Romanovs were Russia's ruling family until the Russian revolution in 1917. They disappeared from history, and were widely thought to have been brutally executed by the Bolsheviks. Remains presumed to belong to some members of the Tsar's family were found in 1918 and reburied, although their identity was uncertain. However, the remains of two of the Tsar's children were not found in this mass grave. The putative Romanov remains were exhumed in the 1990s to see if they could be definitively identified. Part of the identification process of the bones included taking DNA samples from them. Prince Philip, the Duke of Edinburgh, is a maternal-line relative of the last Tsarina of Russia and thus shares his mitochondrial DNA (mtDNA) with her (as this is passed from mother to child). When the mtDNA sequences of Prince Philip, the Tsarina and her children were compared, they turned out to be a match. This strongly suggested the family group were the Romanovs.

The missing bodies of two of the youngest Romanovs fostered the myth that some members of the Tsar's family had survived (most famously the Tsar's daughter, Anastasia), with several Romanov impersonators popping up as recently as the 1980s. Historical reports of the burial of the missing Romanovs allowed archaeologists to track down the site where the two bodies were likely buried and study the remains. The discovery of dental fillings made of silver amalgam in the teeth suggested that the bodies belonged to aristocrats, another piece of evidence supporting the hypothesis that they were the missing Romanovs. With the DNA identification of the large family group, the Romanov remains could be respectfully buried and their ghosts laid to rest.

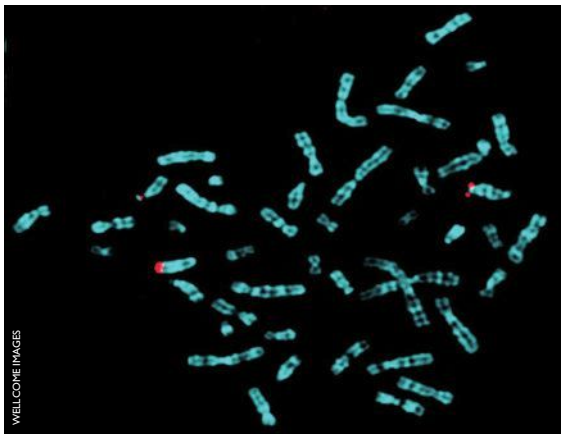
DNA technology was central to the identification of the body of Richard III by scientists at the University of Leicester. His identity was established by finding two living descendents of Richard's mother and sister, who carry the same mtDNA as the monarch. A multi-disciplinary approach was used to identify the skeleton by additional methods, drawing on classical archaeological techniques such as



King Richard III's skeleton was found buried under a carpark in Leicester

the position of the bones in the grave–in this case, with hands apparently bound before him. Osteology (the analysis of bones) revealed a distinct curvature to the spine of the skeleton. This was diagnosed as scoliosis by Cambridge University's Piers Mitchell, a relatively common condition that would have developed while the last Plantagenet king was a teenager. The wounds on the skeleton suggested a violent death, possibly in battle.

Chemical methods were also key to identifying the bones as belonging to Richard III. Direct radio-carbon dating of the bones gave an idea of their age and isotope analysis suggested what kind of diet the individual would have had. Both methods work on the principle that as we grow and consume food, we absorb radioactive material from our environment in the form of carbon and nitrogen isotopes, which slowly lose their radioactivity at a regular rate over time. These techniques informed scientists that the bones were from the right age–late 15th century–to belong to Richard III, and also belonged to someone who ate a much better diet than your average medieval peasant–the diet of a high-status nobleman. Finally, experts performed facial reconstruction at Dundee University to bring the skull 'back to life'.


WELLCOME IMAGES

Technology normally deployed in modern medicine to detect cancers and head injuries was used to confirm the identity of an embalmed head reputed to be that of Henri IV of France. Henri was embalmed and buried in 1610, but didn't rest in peace for long. Amidst the uproar of the French Revolution, many dead kings were dug up in the 1790s and the putative head of Henri ended up in the hands of private owners, most recently in the attic of a retired tax collector!

An X-ray computed tomography (CT) scan is normally used to create a 3D X-ray of tumours, bone fractures or bleeding on the brain. A team of forensic specialists, headed by Philippe Charlier, used CT scanning to look underneath the embalmed soft tissue of the head to the bones underneath. By comparing their scans to busts and portraits of the king, they identified key aspects of bone structure with strong similarity to known images of Henri IV. They were even able to identify a blemish on the side of his nose, visible on both the portrait and the embalmed head, and evidence of a pierced ear. The state of the embalmed head's dental health and baldness also matched with descriptions of King Henri IV.

However, recent DNA evidence has muddied the waters. One study found a match between DNA found from the embalmed head and blood samples purported to come from one of Henri IV's descendants, Louis XVI of France. However, a second DNA test against living descendants of France's royal family, the Bourbons, didn't match that of the embalmed head. However, over 400 years it is possible that contaminating DNA has obscured the real genetic profile of the skull, and that researchers were simply amplifying the DNA of the many people who must have handled the head since its owner's death. In such a situation, with no uncontaminated DNA samples available, only the physical evidence from the head can be used to draw firm conclusions–enough for Henri IV's head to be interred in the cathedral of Saint-Denis, France.

Alfred the Great, 9th century king of Wessex (south-western England), is the latest 'lost royal' to be given the 'CSI treatment'. His bones were moved several times after his death, being ultimately lost somewhere in the grounds of Hyde Abbey, near Winchester. The abbey has a long history of upheaval, first by Henry VIII in the 1500s, and later when a prison was built on the site. It was assumed that Alfred's bones were dumped in a mass grave in the 18th century. Researchers at Winchester University considered this a promising last resting place for Alfred, but radiocarbon dating showed that the bones from the mass grave were 400 years too young to be the Wessex king. They are now examining a pelvic bone excavated on a previous dig which is thought to be from the correct period. With little other skeletal evidence, the chances of unequivocally identifying the remains as belonging to Alfred seem slim. The lost king of Wessex, while Great, may have to remain anonymous.


PUBLIC

King Henri IV's embalmed head was identified using cutting-edge medical technology

DNA contamination of historical samples can mask the genetic identity, giving conflicting results

Charlotte Houldcroft is a temporary lecturer at the Department of Archaeology and Anthropology

Frederick Sanger

Virginia Rutten reviews the life of Frederick Sanger, the British Biochemist and double Nobel Prize winner

Sanger's sequencing technique allow us to read DNA sequences

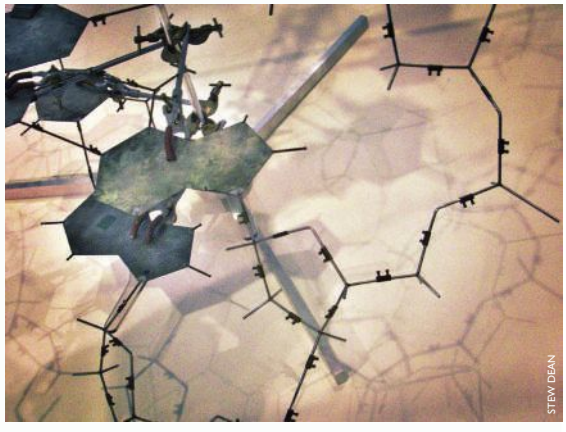
Frederick Sanger, the father of the genomic era, died peacefully last November. He left his legacy: a revolutionised field of biology. This article attempts to describe his life, his achievements and their wide-reaching impact.

Sanger was born in 1918 into a Quaker home in Gloucestershire. He inherited his father's love for science and at 18 he gained a scholarship to study Natural Sciences at St John's College in Cambridge. Struggling in Maths and Physics, he decided to enrol on a newly-founded course: Biochemistry, in which he excelled, graduating in 1939, as war began.

A conscientious objector to battle, he spent the days of conflict in Cambridge carrying out research on nitrogen uptake in root vegetables. In 1943, he continued his studies in Cambridge with a challenging postdoctoral research project investigating protein structure. At the time, the understanding of proteins was in its infancy. People knew they were made of amino acids, but how these were arranged was subject to hot debate. Some thought their arrangement was variable, whereas others, like Sanger, were convinced the order and composition of the amino acids were fixed and unique. When Sanger applied for funding to the Medical Research Council (MRC) to study the sequences of amino acids that make up a protein, his proposal was considered futile and denied. Eventually, he obtained enough smaller grants and began working with one particular protein: insulin.

Insulin is a peptide hormone, secreted by the pancreas, which switches on anabolic, reserve-making metabolism. People who suffer from Type 1 diabetes are unable to produce insulin, and at that time children with this disease would starve to death as their bodies could not utilise nutrients. When this vital protein was discovered in 1921, significant international efforts were made to isolate it, eventually leading to techniques that enabled its separation and purification on a large scale. This gave Sanger the substrate he needed: a pure, cheap and short-chain protein.

Sequencing proteins was not an easy task. Proteins are chains of different types of amino acid units. To find out which amino acids are in the chain, and in what order, the protein must be cut, and the fragments isolated and identified. The difficulty is that there was no way of knowing where this cut had been made as all the bonds linking the amino acids together are identical. To solve this, Sanger



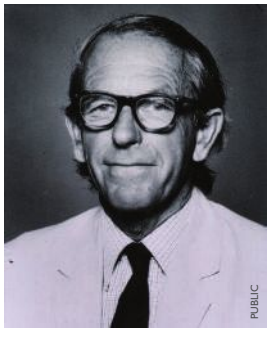
invented a technique called the 'N-terminal labelling technique' which marks the start of the chain, which always contains a nitrogen group, with a detectable compound. The protein is then cut once and the resultant fragments separated; the fragment with the bound detectable compound is now known to be from the beginning of the sequence. This can be repeated and allows sequential identification of all the amino acids in the chain and their position.

After 10 years of hard work, Sanger obtained the full sequence of 51 amino acids that constitute insulin. This new method revolutionised the study of proteins and the Nobel Committee were swift to recognise the value of his work, awarding him his first Nobel Prize in 1958, just three years after his publication.

In the mid-1960s, Sanger launched himself into a new project: decrypting genomes–the whole DNA content of an organism. Francis Crick and James Watson had discovered the double-helix model of DNA and its complementary nucleotides in the early 1950s, but no direct link had been established between DNA and protein sequence. They had discovered the book of life but could not read it. Scientists knew that DNA, like proteins, had a chain-like structure. The challenge was to determine the order of adenine, thymine, guanine and cytosine–the chemical units from which DNA is made.

Sanger was already familiar with RNA sequencing, which he worked on during the late-1950s, and this gave him a head start. He combined established methods with novel ones and developed a ground-breaking way of sequencing DNA: the 'dideoxy chain-termination' reaction. In 1977, using this technique, he sequenced the first

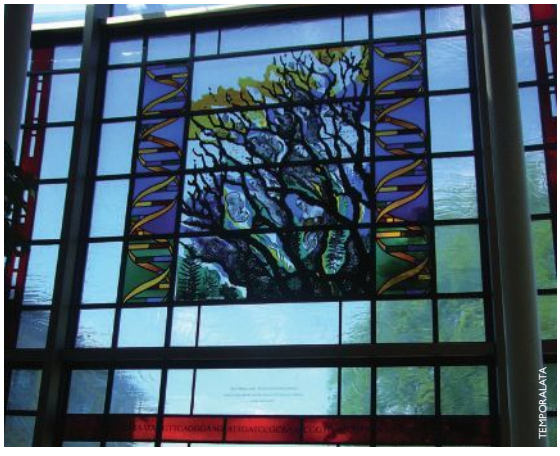
Frederick Sanger was a biochemist who studied in Cambridge for many years



genome of a virus called phiX174.

His method's elegance is in its simplicity. It uses the natural process of DNA replication, which is stopped prematurely with a special terminator molecule. In the first round, a terminating adenosine is added to the reaction. As DNA gets copied, this terminator will eventually become incorporated at every 'adenosine' place of the DNA producing strands of varying lengths, all of which have an adenosine at the end. The process is repeated with terminating thymine, guanine and cytosine nucleotides. In the end, DNA strands of all lengths are produced, each terminating with a known A, G, C or T, spelling out the full sequence! In 1980, again only three years after the publication of the technique, Sanger was awarded his second Nobel Prize.

The 'Sanger method' has now been enhanced and automated using fluorescent nucleotides and laser scanners, and has unravelled the 3 billion base pairs of the human genome. However, it was Sanger's seminal technique that paved the way to understanding the chemical basis of the genetic defects and the basis of inherited disease, some of which we can now screen by simply reading the patient's DNA. Diseases, such as cancer, arise from mutations in the DNA. Modern DNA sequencing techniques tell us where these mutations are, and allow the development of more targeted drugs. By knowing the sequence of proteins we can now synthesise them ourselves, or transport the coding DNA into bacteria which then make the product for us. This has stemmed an explosion in therapeutic possibilities, such as hormone replacement therapy and the development of new antibiotics.



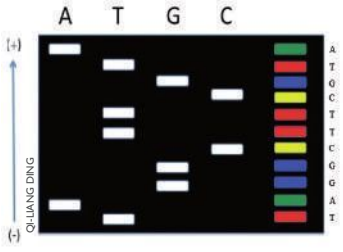
A stained-glass window inspired by DNA was installed at the Wellcome Trust Sanger Institute, in Cambridge

Beyond its vast medical implications, reading DNA is of great use to many other fields: palaeontologists have been able to confirm and map out more accurately the tree of evolution, criminologist use DNA evidence to confirm the presence of individuals in crime scenes and governments verify the contents of meat and foodstuffs, to name only a few examples.

At the age of 65, Sanger left his well-worn bench to retire to his family. He lived the last years of his life tucked away in the Cambridge Fens, practising carpentry, 'messing about in boats' and devoting himself to his family and garden. He outlived his wife, Margaret Joan Howe, after their 72 years of marriage. Although not a scientist herself, he described her as having "contributed more to [his] work than anyone else by providing a peaceful and happy home".

Frederick Sanger impressed the scientific world with his novel techniques and disarming modesty. He referred to himself as "the chap who messed about in his lab" and declined the offer of a knighthood because he did not want to be called 'Sir'. In 1993 he agreed for a research institute in Cambridge to be named after him, but only on the proviso that "it had better be good!"

Sanger's techniques of protein and DNA sequencing propelled biology forward. His story illustrates how science often lingers, waiting for new technology to broaden its horizons. Indeed, exponential advances in science follow as often from the discovery of new experimental techniques as from the formulation of novel ideas. Just as the invention of the telescope opened up the universe to Galileo, and the microscope a new world of cells and bacteria, Sanger's method offered us a new set of glasses: a pair that enabled us to begin understanding the genetic code.



The 'dideoxy chain-termination' method relies on halting DNA elongation with one of four detectable building blocks, revealing their position in the chain

Virginia Rutten is a 2nd year medical student at Trinity Hall

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Stem Cells: with great power comes great responsibility

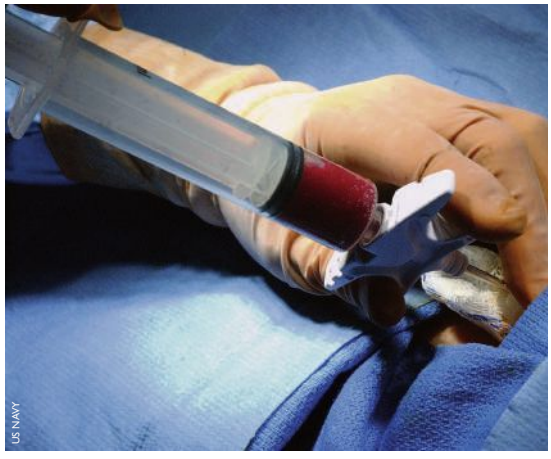
Alessandro Bertero discusses the controversy behind stem cell therapies

Stem cells have the potential to divide itself indefinitely and to differentiate into any cell type

THE TERM 'STEM CELLS' has become one of the most widely-used scientific expressions of our time, and the extreme popularity of stem cells in the media has established them as a part of modern culture. As a result, everyone seems to know what a stem cell is, and what a stem cell can do. Nevertheless, some clarification can be of particular use in this case, as the social and political implications of stem cell use are growing increasingly complicated.

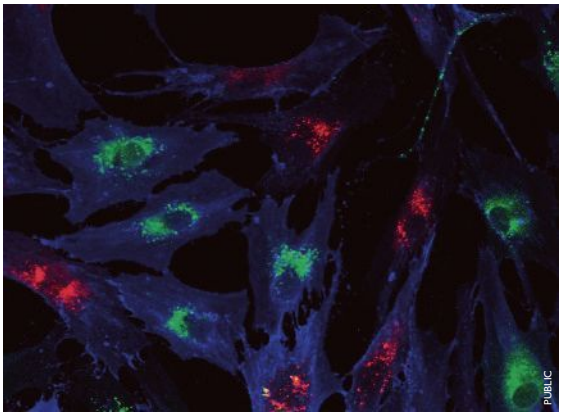
A stem cell has the potential to divide itself indefinitely and to differentiate into any specialized cell type. Over the last few decades, researchers have discovered many types of human stem cells that can be found throughout development and adult life. Theoretically, cultivation and differentiation of stem cells under specific conditions in laboratory settings offer the chance to generate nearly unlimited copies of any cell type of the human body, hence presenting the possibility of replacing faulty or deceased cells with healthy ones. However, the leap from acknowledging these opportunities to believing that humankind had found a long-life elixir was, for the media and the public, unrealistically short.

Overwhelming coverage in the media has led the public to believe that in the near future, terrible



Bone marrow replacement is one of few applications of stem cell therapy currently available

diseases like Alzheimer's, cardiac failure and diabetes will be cured. However, several years down the line, the hype of stem cell therapies has proven to be excessive. In fact, most stem cell based cures are still going through laboratory and clinical evaluation, with the exception of a few notable applications in corneal, skin and bone marrow replacement.



Given the complexity involved in developing such therapies, this delay may be unsurprising to most scientists, but is having dangerous effects on the wider public.

Private clinics around the globe have been instilling false hope in a growing number of patients, promising miraculous stem cell based cures. Instead of losing faith in the clinical applications of stem cells, more and more people have started to look for these therapies outside the evidence-based medicine, in particular victims of devastating diseases for which 'conventional' medical practice provides no definitive treatment. These controversial 'therapies' are most notably offered in India, Japan, China, Mexico and Costa Rica, in which the regulation for the use of stem cells is very loose, often allowing unaccredited laboratories to offer putative treatments for autoimmune, neurological, metabolic and even genetic disorders. The resulting predicament has been described as 'stem cell tourism', and its social and medical complications are growing. Well-documented cases of patients getting severely worse vastly outnumber the few sporadic and dubious reports of miraculous outcomes.

This phenomenon reflects the general public's deep ignorance of stem cell research, and it is the people responsible for educating and protecting patients who are to blame. Scientists, journalists and governments have all contributed to this misinformation by failing to accurately communicate the reality and limitations of stem cell technology. This is one of several examples of modern scientific discoveries, in which the will to justify huge public research investments

has overshadowed the need for accurate scientific divulgation. Indeed, a similar situation occurred when the human genome was first sequenced in 2001. This crucial milestone was welcomed by premature claims of having found the key to cure all human diseases, but after more than a decade of research, we are still unable to fully understand most of the information encoded in our DNA.

More recently, the confusion between the fact and fiction of stem cell therapy has resulted in multiple private companies and lobbyists trying to bring the flux of 'stem cell tourists' back to the US and Europe, by attempting to subvert local regulation regarding stem cell use. An emblematic case happened in Texas in 2011, when Governor Rick Perry supported the loosening of stem cell legislation. By categorising stem cell therapies as tissue transplants instead of biological drugs, the new state rules allowed several companies to bypass the federal law requirement for clinical trials before treating patients. Perry himself became the first patient of one of these companies, Celltex, and was hence accused of having a conflict of interest, despite not being a shareholder. The new regulation led to a legal dispute that eventually halted most of these procedures and stirred a polarising public debate, where the understandable emotional considerations of patients claiming their right to decide their own treatment quickly overwhelmed legal and scientific arguments.

A very similar scenario is happening in Italy, where the so-called 'Stamina method' is dividing public opinion. The procedure has been repeatedly stopped due to growing concerns regarding its safety, methodology and therapeutic rationale, but then re-authorised by sentences from local courts, backing ferocious public protests that claim the right of patients to be treated.

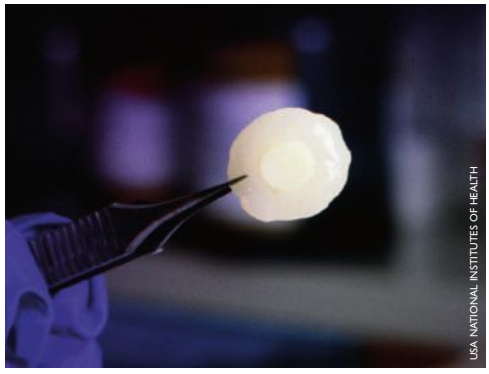
Apart from providing more evidence that better communication of facts in stem cell research is mandatory, these cases also reflect another controversy in the field. For the first time, public attention is being drawn to the scientific and legal debate on how stem cell therapies should be regulated. A growing number of scientists are starting to believe that the current legislation might not be completely appropriate. For example, some claim that rules originally established for chemical drugs do not take into account the intrinsic differences between normal medication and stem cells. The dilemma of complying with the strict normative guidelines of the so-called 'Good Manufacturing Practice' when dealing with stem cells is regarded by some as a major obstacle in the development of novel therapies. Moreover, it is important to realise that pre-clinical studies of efficacy in animal models might be particularly

Governor Rick Perry's support for looser stem cell legislation allowed several companies to bypass clinical trials

inappropriate when studying human stem cells. Another opposing argument is that clinical trials with stem cells are often approved only in patients that are in a very late stage of illness. This reduces the chances of a therapy to show efficacy (it can be argued that many of the now established stem cell therapies would not have been approved within the current legislation) and prevents other patients from accessing such trials because they are, paradoxically, 'too healthy'.

Legislation itself has also been blamed for the rising rate of 'stem cell tourists'. Some people argue that patients are getting so frustrated with the lack of access to 'canonical' stem cell clinical trials that they turn to other stem cell sources. Even from a neutral standpoint, it is clear that proposed changes in stem cell legislation should not be considered taboo; they should be carefully and logically evaluated for pros and cons, as well as applicability and feasibility.

It is rare for fields in medicine and science to reach such a level of publicity and controversy as stem cell therapy has received. With many therapeutic milestones already achieved, and several others in close reach, stem cell technology presents one of the greatest opportunities for humanity to eventually treat numerous devastating diseases. However, as with any great power, the use of stem cells comes with great responsibility. It is now apparent that the path towards the safe therapeutic application of stem cells is a tightrope-walk rather than a downhill-race. Indeed, we must inform public opinion about the scientific facts of stem cells, as well as scrupulously maximise the potential of this technology while carefully protecting patients. The prize is big, as are the potential pitfalls–the game is on.



Mesenchymal stem cells can produce cartilage (shown above), bone and fat, and are allegedly used in the 'Stamina method' to treat a host of diseases

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Weird and Wonderful

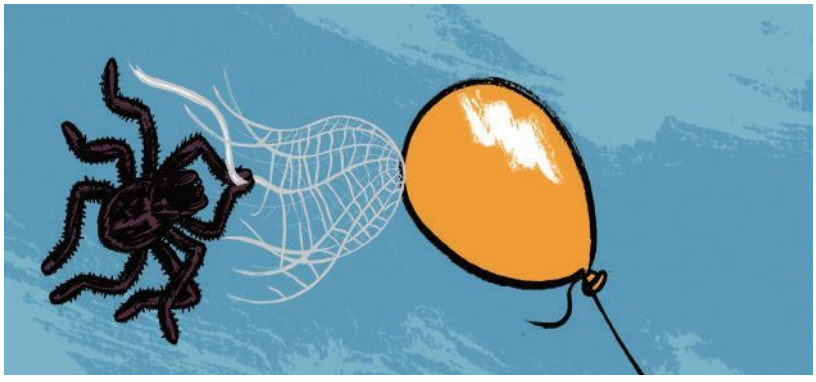
A selection of the wackiest research in the world of science

Human chimeras

IF A CHILD takes a blood test and is found to not genetically match the father, it doesn't take a detective to figure out why. But what if the mismatch is with the mother? This is the case of Karen Keegan and the curious peculiarity of the 'human chimeras'. Suffering from renal failure, Karen was in need of a kidney transplant. Her husband and two oldest children gave blood samples to see if they would be a match. To everyone's surprise the children did not relate genetically to her, although they did to the father. Further tests showed that, even though her blood DNA did not match her child's DNA, the DNA gathered from her organs did. The solution? Karen isn't technically one person: she's two! During Karen's conception two spermatozoon fertilised two eggs, producing twins. In the course of the pregnancy, the embryos fused, and each of them developed in different areas of her body. This phenomenon, known as 'Chimerism', has been recorded in several cases around the world. The twins can even be of different sex and this can produce hermaphroditic individuals. As for Karen, though none of her children matched, it was found that her husband was a suitable donor and she is still alive today. **NS**

Spider's web aren't just sticky: they're staticky!

A TEAM LED BY FRITZ VOLLRATH at the University of Oxford have discovered that the glue across the surface of spider webs conducts electricity. The article published in *Naturwissenshaften* late last year describes how the electrostatic field across a web causes it to reach out and grab any charged particle that comes close enough. As a result, pollen, airborne droplets and insects are all fair prey. Based on this experimental finding, Vollrath and his team modelled two possible consequences. First, they proposed that the electrostatic field of a web should cause a small, local disruption in the natural electric field of the Earth itself. Most flying insects should be able to detect changes in local electric fields through movements in their antennae, and so it is possible that an approaching insect could sense the presence of a web in this way. However, whether an insect would have enough warning to evade the web before it snares them is yet unclear. Another conclusion of the article is that spiders' webs could catch airborne pollutants such as pesticides and fertilisers. This could make it possible to measure pollutant levels in a particular area by using webs as natural sensors. Bad news for house-proud spiders and arachnophobic environmental scientists alike. **CA**



It's peanut butter jellyfish time

A WHOLE NEW MEANING has been given to the infamous peanut butter and jelly sandwich, with scientists at the Dallas Zoo creating the world's first peanut butter jellyfish. Two hundred and fifty baby moon jellyfish were fed a mixture of peanut butter and salt water twice every 24 hours. Within 8 days of 'peanut-butterification' the jellyfish had grown significantly and turned brown. They even resembled peanut butter cups! "We just wanted to see if it could be done," said scientists Montoya and Christie. "Whether or not it should be done is a question no doubt to be debated by philosophers for years to come (or at least by some aquarists over beers)", they mused. Although experimenting with the popular spread may have started as some light frivolity, the results could have important implications for aquaculture. Aquatic invertebrates are notoriously difficult to keep in captivity and their dietary requirements differ significantly from the average goldfish. Finding a novel, inexpensive protein source to replace the unsustainable fish and shrimp-based feeds currently used has been a focus of research for some time. While comprehensive studies have yet to be conducted, the lucky jellies in this study appear to have thrived as well as those fed a traditional diet. Closing comments from the scientists implied an additional philanthropic agenda to their research, stating: "We feel that becoming one with peanut butter helps them fulfil their ultimate destiny–to become peanut butter and jellyfish!" **MS**

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