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FRANCESCO BONGIORNI

The impossible dream

Sometimes science needs to take a step back from the facts

HOW does science advance? The number of papers published annually doubled every 9 years in the second half of the 20th century; the number of working scientists now doubles roughly every 18 years. So we might expect science today to be advancing at a breakneck pace. And so it is, but in a great many small steps, rather than giant leaps of understanding.

That's fine: science has always advanced in small steps, paving the way for occasional leaps. But sometimes fact-collecting yields nothing more than a collection of facts; no revelation follows. At such times, we need to step back from the facts we know and imagine alternatives: in other words, to ask "what if?"

That was how Albert Einstein broke the bind in which physics found itself in the early 20th century. His conception of a scenario that received wisdom deemed impossible – that light's speed is always the same, regardless of how you look at it – led to special relativity and demolished what we thought we knew about space and time.

Now physics finds itself at an impasse again – and some physicists are reimagining the impossible, from revisiting the speed of light to dreaming up antimatter worlds. Their hope is that such what-if scenarios may provide coherent explanations for facts we have diligently collected but don't understand (see page 28).

Physics isn't the only field that might benefit from a judicious dose of what-ifery. Attempts to understand consciousness are also just inching forward. We know anaesthetics can turn our awareness off, but not how they do so. What if the answer lies not in their chemistry, as is usually thought, but in physics (page 36)?

Despite its dependence on hard evidence, science is a creative discipline. That creativity needs nurturing, even in this age of performance targets and impact assessments. Scientists need to flex their imaginations, too.

"Let us dare to dream," the chemist August Kekulé once suggested, "and then perhaps we may learn the truth." ■

Should have sent a poet

FROM the Earth to the Moon. In Jules Verne's 1865 novel, a group of energetic American plutocrats embark on a private moonshot, firing three intrepid explorers out of a vast cannon in Florida.

Cannons may not feature much at NASA, but Verne's book proved prescient: in its sequel, the capsule orbits the moon before returning to splash down at sea, just as Apollo 8 did a century later.

What of the human dimension? SpaceX founder Elon Musk is a cult figure; his works are followed avidly – as were those of Verne's plutocrats. Speculation is already rampant over the identities of the wealthy would-be astronauts.

Musk has said they aren't "from Hollywood". Perhaps that's where Verne finally gets it wrong. His third lunar explorer was a poet, standing for human experience beyond the hard-nosed and well-heeled. Or just possibly life will imitate art once again. ■

California under water

THE strongest storms California has seen in years have been drenching the state after five consecutive years of drought. Rainwater has filled reservoirs to the brim - with excess escaping down dam spillways or lapping over levees for the first time in decades - and there has been flooding up and down the state.

The drought and floods can be traced to the bands of water vapour being carried up from the tropics, says Michael Dettinger of the US Geological Survey. California gets almost half its rain from these "atmospheric rivers", but they brought fewer storms than usual to the West Coast over the past few years, causing drought. This year, however, there have been close to 30 such storms already, says Dettinger.

Years of drought have dried up hillsides and killed vegetation, creating the right conditions for mudslides and flooding, says Lynn Ingram of the University of California, Berkeley.

Historically, California often sees periods of drought punctuated by years of intense flooding, she says. "The past really is telling us to prepare for both extremes," she says.

The Sierra Nevada mountains now have 160 per cent of their normal snowpack, a welcome resource. But there will be little room for extra meltwater this year, which may mean further floods.

The state's water infrastructure is also ageing. Whether the dams and levees will hold under the strain is a concern, Dettinger says.



Heavy floods followed drought

Microbe danger list

THE World Health Organization has named the bacteria we most urgently need new antibiotics for, as they grow increasingly resistant to the ones we have. Among those at the top of the list are gut bacteria such as *Escherichia coli* – a deadly threat in hospitals.

The WHO's list is aimed at a meeting in Berlin this week of health ministers from the world's 20 richest countries. They will discuss funding drug firms to develop new antibiotics, which

the University of Tübingen, Germany, pinpointed the most damaging families of drug-resistant bacteria based on criteria such as how often bacteria resist antibiotics, how many they resist, how often they kill and the number of people affected.

The most crying need is for drugs to kill *Acinetobacter*, *Pseudomonas* and members of the Enterobacteria family that resist the last-resort carbapenem antibiotics. The Enterobacteria include *E. coli*, which takes a heavy toll in hospitals and nursing homes, where it can cause fatal blood and lung infections.

E. coli is also the cause of most urinary tract infections, one of the most common infections requiring antibiotics – half of all women have a UTI at least once in their lives.

Effective antibiotics make most UTIs only a minor annoyance, but if antibiotics fail, the infection can spread into the kidneys and bloodstream, and even become life-threatening. Many UTIs now resist one or more types of antibiotic, and a few have resisted all of them.

"Current work on new antibiotics focuses on easy bacteria, not those doing the most harm"

are otherwise too unprofitable to invest in.

Priorities need to be spelled out, says Nicola Magrini of the WHO, partly because current work on new antibiotics is largely aimed at the bacteria for which it is easiest to find and test new drugs, not those doing the most harm.

Researchers at the WHO and at

Nerve gas killing

WAS Kim Jong-nam really assassinated with a nerve agent? The exiled half-brother of North Korean dictator Kim Jong-un was killed at Kuala Lumpur airport in Malaysia on 13 February after two women ambushed him and wiped something on his face.

Malaysian authorities have said Kim was killed with VX nerve agent, but chemical weapons experts are less convinced. VX is the most toxic substance known – 10 milligrams of the oily liquid on

your skin is lethal. But Kim took some time to show symptoms, which include convulsions and frothing at the mouth. What's more, the poison was handled by unprotected assailants and didn't contaminate other people.

But it might just be that VX from North Korea – which is suspected of carrying out the attack – is losing its punch. The substance is thought to have been synthesised some years ago using precursors from abroad. Tests on Iraq's VX after the 1991 Gulf war showed that it degrades over time.

Plain packets help smokers quit

THE proof is in the packaging. Making all cigarette packets look the same encourages smokers to quit. These findings come ahead of the introduction in May of plain tobacco packaging in the UK and Ireland.

Australia was the first nation to introduce such legislation in 2012. All cigarettes are now sold in plain olive packets with standard fonts and graphic health warnings.

The primary goal was to make cigarettes less appealing so people

wouldn't take up smoking in the first place. But an added bonus has been the number of existing smokers who have ditched the habit. Between 2010 and 2013, the proportion of daily smokers in Australia dropped from 15.1 to 12.8 per cent – a record decline (*Addictive Behaviors Reports*, doi.org/b2d6).

This drop can be partly explained by a loss of brand affinity, says Hugh Webb at the Australian National University in Canberra.

60 SECONDS

Fly me to the moon

SPACE travel company SpaceX plans to send two private citizens around the moon in 2018.

The two individuals, whose names were not released, will pay an undisclosed but "significant"

"They would be the first people to complete this journey since Apollo 13 in 1970"

amount of money to be the first civilians to circle the moon. Nobody has completed this journey since Apollo 13 in 1970.

SpaceX plans to launch the pair aboard a Crew Dragon craft on a Falcon Heavy rocket, neither of which have yet been tested in space.

The Crew Dragon's first uncrewed test flight to the International Space Station is scheduled for November, and its first crewed flight is set for May 2018. The first Falcon Heavy launch is planned for early 2017.

Given that the spacecraft haven't been fully tested yet, a crewed launch in 2018 seems an optimistic timeline.

"It's typical SpaceX bravado," says space policy expert John Logsdon at George Washington University in Washington DC. "This is basically a joyride... It doesn't advance any exploration objectives. It's like a very high bungee jump."



The handset that won't die

Going mobile

A VENERABLE mobile phone saw its reputation for survival further enhanced this week. Nokia's reboot of its 3310 model, first released way back in 2000, was the star of annual tech event Mobile World Congress in Barcelona, Spain.

The updated model has a colour screen and camera, but still offers classic game *Snake*. Whether it proves as indestructible as its predecessor remains to be seen.

"The updated Nokia 3310 has a colour screen and camera, but still offers classic game *Snake*"

The event also saw the latest smartphones unveiled, such as Sony's Xperia XZ Premium, the first handset to feature a high-resolution 4K HDR screen. The phone's camera can film at 960 frames per second, allowing you to play videos back in super-slow motion.

Other highlights of the show included robot assistants that could make coffee, give directions and play drum solos, and Bluetooth headsets ready to bring AI assistants like Siri to your ear.

Meanwhile, a fleet of driverless cars were parked around the auditorium, including racing championship Roborace's first

self-driving race car. And connected "internet of things" devices were everywhere, from delivery trucks to hard hats, pallets, wine bottles and even mousetraps.

No surprise, then, that the development of a 5G mobile network needed to support such a data-hungry future was a key focus of the event.

Wood as bad as coal

EUROPEAN UNION nations, including the UK, may be wasting money by subsidising the burning of wood for energy.

While burning some forms of wood waste can cut greenhouse gas production, the growing use of wood energy in the EU is raising rather than reducing emissions, a report concludes.

Overall, burning wood for energy is much worse in climate terms than burning gas or even coal, partly because it reduces the amount of carbon stored in forests. However, a loophole in EU law means that emissions from wood burning can be ignored, concealing the damage, it says.

"It is not a great use of public money," says report author Duncan Brack of Chatham House, a policy research institute in London. "It is providing unjustifiable incentives that have a negative impact on the climate."

Eco-unfriendly cuts

The US Environmental Protection Agency could be a big loser from President Trump's first budget proposals. Its funding and staffing could be slashed as part of wider cuts to boost military spending by \$54 billion, according to reports citing officials. If they go through, programmes to protect air and water quality could be affected.

Crewed test possibility

NASA plans to study whether it would be feasible to put astronauts on the first test flight of the Space Launch System booster rocket, it announced last week. The SLS is currently scheduled to send an uncrewed Orion capsule into orbit in late 2018, and a crewed capsule in late 2021.

Self-driving lawsuit

Google's self-driving car company Waymo is suing Uber, accusing the ride-sharing firm of stealing its lidar technology - the laser system that lets self-driving cars chart their surroundings. Waymo claims that a former employee stole designs before going on to co-found self-driving truck start-up Otto, which Uber bought last year.

Humans spark wildfires

Five out of six wildfires in the US over the past two decades were triggered by people, a new study finds. Human activity makes the wildfire season start earlier in the east and last longer in the west, outdoing climate change in terms of making fires worse (*PNAS*, doi.org/b2fb).

Obesity cancer link

Being overweight raises your chances of getting certain major types of cancer, a meta-analysis of obesity studies and cancer risk has found. People with a high body mass index were more at risk of developing oesophageal, bone marrow and kidney cancers, among others (*BMJ*, DOI: 10.1136/bmj.j477).



Gene therapy breakthrough

For the first time, gene therapy has treated a common genetic disorder, finds **Andy Coghlan**

A TEENAGE boy with an inherited disease that affects millions worldwide seems to have been cured using gene therapy. The treatment appears to have stopped the painful symptoms of sickle cell disease, demonstrating the potential for gene therapy to treat common genetic diseases.

The idea of gene therapy – using strands of DNA to compensate for a person's malfunctioning genes –

"All the blood tests we performed show that the teenager has been cured of sickle cell disease"

is almost three decades old. However, the approach has so far mostly been used to treat very rare diseases (see "Long road to success", below). In contrast, sickle cell disease affects 100,000 people in the US alone. If the treatment proves successful in larger trials, it could bring gene therapy into widespread use.

"It could be a game changer," says Deborah Gill at the University of Oxford. "The fact the team has a patient with real clinical benefit, and biological markers to prove it, is a very big deal."

People with sickle cell disease make abnormal versions of haemoglobin, the blood protein that carries oxygen around the body. This can be caused by mutations in the gene that makes a subunit of haemoglobin, called beta-globin. The mutations cause haemoglobin to clump together, distorting red blood cells into a sickle-shape that can get stuck in blood vessels around the body.

People with the disorder are

given blood transfusions to clear these painful blockages and prevent new ones. Bone marrow transplants can treat the disease, but matching donors can only be found for around 10 per cent of people with the condition.

Now a team in France seems to have developed a treatment that would work for everyone with the disorder. First, the team took bone marrow stem cells from the boy when he was 13, and gave them extra, mutated versions of the gene that codes for beta-globin. These were designed to make beta-globin that would interfere with the boy's faulty proteins, stopping them from clumping together.

The researchers then put these stem cells back into the boy's body. After around three months, he began producing large quantities of haemoglobin that behaves normally (*New England Journal of Medicine*, DOI: 10.1056/NEJMoa1609677). "The patient is now 15 years old and free of all previous medication," says Marina Cavazzana at the Necker Children's Hospital in Paris, who led the team. "He has been free of



Many rely on blood transfusions

pain from blood vessel blockages, and has given up taking opioid painkillers."

Cavazzana is confident these benefits will last. "All the tests we performed on his blood show that he's been cured, but more certainty can only come from long-term follow-up." She says her team has treated seven other patients, who are showing "promising" progress.

"We are all very excited by the work, and this success provides

support for this and other genetic strategies targeting this horrible disease," says John Tisdale at the US National Heart, Lung, and Blood Institute in Maryland.

David Williams, at Boston Children's Hospital in Massachusetts, suggests that the boy may still occasionally experience blockages, because his own original genes are still able to produce faulty haemoglobin. "It's important to see what happens over time, and how many other patients see similar benefits."

However, should the gene therapy prove to be effective in larger trials, its expense may limit its use to richer nations. "We should be realistic in remembering that there are hundreds of thousands of sickle cell patients in less developed countries, and that the therapy is not easily exportable or adaptable to countries with less well-developed health systems," says Stuart Orkin at Harvard Medical School. ■

LONG ROAD TO SUCCESS

Twenty years ago, gene therapy was touted as a cure for everything from cancer to cystic fibrosis. Now it is finally starting to fulfil its promise.

In 2012, Glybera became the first gene therapy to be approved, for people with a rare disorder that makes them unable to process dietary fat. Last year, the first commercial gene therapy that alters a person's DNA was approved for children with a

severe immune disorder. Gene therapies for rare forms of blindness are also showing promise.

But these conditions all affect very small numbers of people. Research into sickle cell disease (see main story), beta thalassaemia, haemophilia and cystic fibrosis mean gene therapy may not be too far from becoming mainstream medicine for the most common genetic diseases.

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That fingernails on slate feeling has a name

YOU may not have heard of "*grima*", but you've almost certainly felt it. Spanish speakers say they feel *grima* when they hear the sound of fingernails on a blackboard. Now psychologists are suggesting *grima* is distinct from other emotions.

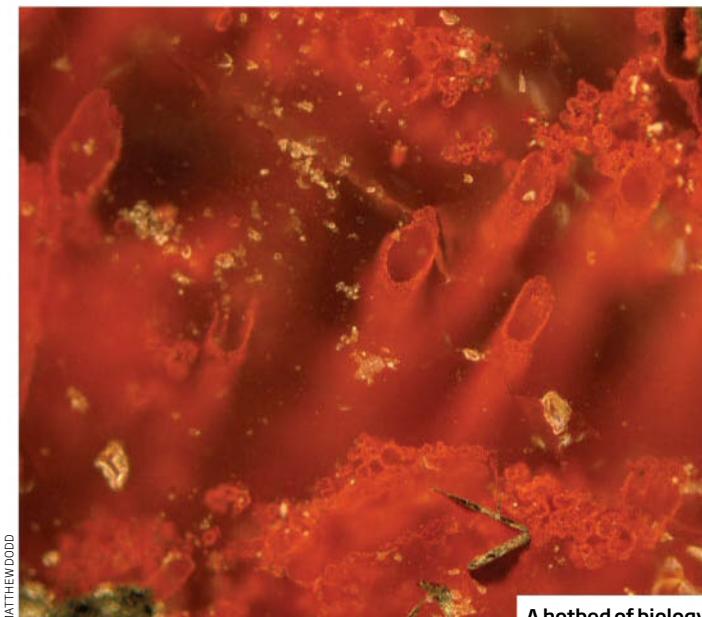
Inge Schweiger Gallo at the Complutense University of Madrid has personal reasons for studying *grima*. "For as long as I can remember, I've had problems touching foam rubber," she says. "Whenever I have to use it, for example, in packages, I try to ask somebody else to touch it for me."

Schweiger Gallo and her team asked Spanish speakers what *grima* means to them. They most frequently mentioned an "unpleasant sensation", "shivering", "sounds" and "repulsion". Stimuli that elicited *grima* included squeaking noises, scratching with fingernails and scratching on surfaces. The volunteers rated *grima* as being less pleasant than disgust.

Next, the team turned to German and English speakers, who have no word for *grima* in their languages. When they heard *grima*-eliciting sounds, the volunteers' heart rates fell slightly, then rose sharply, before returning to normal after about 6 seconds. Sounds labelled as disgusting or unpleasant showed a different pattern. But the changes in skin conductance - a sign of a physiological response - were similar for *grima* sounds and disgusting or unpleasant sounds.

When Spanish volunteers tried to suppress their responses to *grima*, they rated *grima* sounds as less unpleasant. But this didn't work for disgust-inducing sounds (*Frontiers in Psychology*, doi.org/b2d7). This indicates *grima* is not a reflex reaction, but a distinct emotional experience that can be influenced by thought.

Together, the results suggest *grima* is similar to disgust, but has different triggers and physiological responses - even in people who don't have a name for it in their language. Sam Wong ■



Little tubes could be oldest traces of life yet

ARE we closing in on life's cradle? What's claimed to be the oldest evidence of life on Earth yet found backs the idea that the first microbes originated around hydrothermal vents on the seafloor - but the finding is already proving controversial.

Life must have started some time between Earth's formation 4.5 billion years ago and the appearance of the first undisputed fossils, about 3.4 billion years ago. But exactly when or where it arose remains a mystery.

One promising place to seek clues is the Nuvvuagittuq belt in northern Quebec, Canada. The rocks here, on the coast of Hudson Bay, are at least 3.75 billion years old, and some geologists argue they are about 4.3 billion years old, just slightly younger than the planet itself.

Like all such ancient rocks, they have been heavily altered. At some point they were deep inside Earth, where temperatures above 500°C and extreme pressures baked and deformed them. But geologists can still read clues that

they formed near hydrothermal vents at the bottom of the very early Earth's oceans.

Matthew Dodd at University College London and his colleagues believe they have now found evidence of microbes in these rocks: microscopic tubes and filaments made of iron oxide. Very similar structures are

"It once again gets us thinking about a potential hydrothermal cradle of life"

formed by bacteria that live in mat-like colonies around modern deep-sea hydrothermal vents (*Nature*, DOI: 10.1038/nature21377).

What's more, the carbon in the material close to the filaments has an isotopic balance characteristic of biological processes, says Dodd. Some of that carbon is inside crystals of phosphorus-rich minerals, which also hints at early biology. "Phosphorus is essential for all life on Earth," says Dodd. "As organisms die and decay, it is

released and it can then be incorporated into minerals."

Taken together, the evidence points to one inescapable conclusion, he says: the very early Earth was home to microbes similar to those found around today's hydrothermal vents.

Until now, the strongest fossil evidence for early life had come from shallow water deposits such as beach sands, says David Wacey at the University of Western Australia in Perth. "This study once again gets us thinking about a potential hydrothermal cradle of life." The first organisms would have derived their energy from geothermal processes, since there is little or no sunlight on the ocean floor.

Wacey thinks the team's findings are reasonably solid. "The individual lines of chemical evidence are not particularly strong, but put these together with the evidence from the filaments and one comes up with a pretty convincing biological scenario," he says.

David Emerson at the Bigelow Laboratory for Ocean Sciences in East Boothbay, Maine, is more cautious. "You do get unique structures in these mat communities that are very easily identifiable as biological," he says. "The problem is that when you go back in time it becomes harder and harder to interpret the evidence."

Others are unconvinced. "I am frankly dubious," says Frances Westall at the Centre for Molecular Biophysics in Orléans, France. "All kinds of reactions take place at [high] pressures and temperatures. The filaments might simply be a by-product of those reactions and have nothing to do with life," she says.

The claims by Dodd's team cannot be just dismissed, though. Wacey says many researchers will want to scrutinise the evidence in great detail before making up their minds. "It may be many years before a consensus is reached," he says. Colin Barras ■

Seeking life on new rocky worlds

Leah Crane

WE ARE already taking the first steps toward learning if there could be life on TRAPPIST-1's newly discovered planets – and what that life might look like.

Last week, a team led by Michaël Gillon at Belgium's University of Liege announced that TRAPPIST-1, a small, faint star some 40 light years away, has four more rocky planets to join the three we already knew about.

All are less than 20 per cent bigger than Earth, and all orbit well within the distance at which Mercury circles our sun. Despite this closeness, the planets may be candidates to search for life. That's because TRAPPIST-1 is much smaller and dimmer than the sun, so three of the planets may be cool enough to host liquid water on the surface, putting them in the habitable zone (see diagram, right).

But small, red stars like TRAPPIST-1 can emit powerful flares of X-rays and UV radiation. Too much UV radiation could leave a planet lifeless – and since they orbit so close to their star, TRAPPIST-1's planets are at

particularly high risk.

So astronomers are puzzling out whether life could find a way, and if so how we could spot it.

Lisa Kaltenegger and Jack O'Malley-James, both at Cornell University in New York, examined how well different atmospheres could keep harmful radiation from reaching the surface of those planets in the habitable zone. They found that an atmosphere similar to present-day Earth's would provide enough protection for life as we know it to survive there, even if the star turns out to be one of the most active of its type.

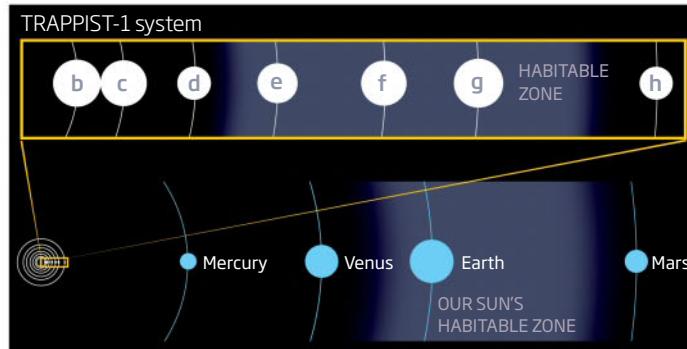
An atmosphere one-tenth as thick as ours would be less effective, letting through similar amounts of UV radiation to what Earth received 2 billion years ago – harsh, but still potentially amenable to life.

An even thinner atmosphere, similar to what Earth had when life arose 3.9 billion years ago, would only allow for life as we know it if TRAPPIST-1 turns out to be calm. If the star flares, any life would have to take shelter under the surface, in oceans or in caves. Such hidden life would be safe, but nearly impossible for us to detect (arxiv.org/abs/1702.06936).

Other means of protection could provide a shining beacon for us to spot. Some corals absorb and re-emit UV light at longer, less-harmful wavelengths, resulting in a blue-green glow.

A world apart

The seven rocky planets orbiting the star TRAPPIST-1 could all fit within the orbit of Mercury. Despite this, three are in the star's "habitable zone"



BPA-free water bottles may be harmful too

TALK about unintended consequences. A chemical called BPA is being phased out of plastic packaging due to fears it may disrupt our hormones – but a replacement for it may be just as harmful.

BPA, or bisphenol A, is often found in disposable water bottles and babies' milk bottles and cups. Small amounts can dissolve into the food

and drink inside these containers.

This is a concern because a host of studies have shown that BPA can mimic the actions of oestrogen, binding to the same receptor in the body. Animals exposed to BPA develop abnormal reproductive systems, but it is unclear if people are exposed to high enough doses to be affected.

Due to public pressure – and bans in a few countries – many manufacturers have started replacing BPA. One substitute, fluorene-9-bisphenol, or BHPF, is already widely used in a variety of materials.

But Jianying Hu of Peking

University, Beijing, and her team have found that BHPF also binds to the body's oestrogen receptors. Unlike BPA, it does this without stimulating them, blocking their normal activity. In tests on female mice, BHPF caused the animals to have smaller wombs and smaller pups than controls, and in some cases miscarriages.

If BHPF binds to the same receptor in humans, it has the potential to

"If BHPF binds to the same receptor in humans, it has the potential to cause fertility problems"

Kaltenegger and O'Malley-James say that similar mechanisms could help organisms survive on planets like the ones around TRAPPIST-1 (arxiv.org/abs/1608.06930).

"Your planet would light up, but so would the ones that you see in the night sky," says Kaltenegger. "Wouldn't that be a beautiful thing to see?"

In another study, Kaltenegger and her Cornell colleague Ramses Ramirez found that volcanic activity that releases lots of hydrogen into the atmosphere could keep a chilly planet warm, potentially extending TRAPPIST-1's habitable zone out to its most distant planet (*The Astrophysical Journal Letters*, doi.org/b2c3).

Researchers are already using the Hubble Space Telescope to look for possible life-supporting atmospheres around six of TRAPPIST-1's planets. Hubble's successor, the James Webb Space Telescope, should be able to follow up with a closer look at their potential atmospheric chemistry.

The planets' coordinated orbits and proximity could make it easy for meteorites bearing water or even life to jump between them. "You would only be required to have biological material on one planet, which would then be shared to the others," says Stephen Kane at San Francisco State University. Additional reporting by Joshua Sokol ■

cause fertility problems. "That's pretty scary," says Frederick vom Saal of the University of Missouri.

Out of 100 college students who regularly drink water from plastic bottles, Hu's team detected low levels of BHPF in the blood of seven people (*Nature Communications*, DOI: 10.1038/ncomms14585).

Vom Saal says even low levels could in theory disrupt our hormonal systems. He says he tries to use plastic as little as possible, and avoids putting plastic containers in the microwave or dishwasher, as they degrade under heat. Clare Wilson ■

208 new rocks back case for Anthropocene

THE evidence that humans are changing the planet is solid as rock. A new catalogue of minerals counts 208 that result solely or primarily from human activity, says Robert Hazen of the Carnegie Institution for Science in the US, who led the study.

This is almost 4 per cent of the 5200 minerals recognised by the International Mineralogical Association. It bolsters arguments for designating a new geological period - the Anthropocene - characterised by human impact.

Most minerals were created about 2 billion years ago during the Great Oxidation, when free oxygen produced by photosynthetic bacteria appeared in Earth's atmosphere. At that time, minerals spiked from just over 2000 varieties to more than 4000. "After that, it really was a kind of plateau," says Jan Zalasiewicz at the University of Leicester, UK. "The next big jump is what humans have been doing."

Humans have manufactured synthetic mineral-like compounds, such as those in silicon chips, bricks, porcelain and metal alloys. New minerals may also be forming in solid waste dumps where old electronics and high-tech discards are exposed to weathering (*American Mineralogy*, DOI: 10.2138/am-2017-5875).

"There are probably all sorts of things forming," Hazen says. "TVs have all these exotic phosphors they use, and magnets and all sorts of high-tech materials. When you start hydrating and oxidising them, you're going to start finding a lot of exotic new materials."

Some minerals in things like cement are rare in nature but are now widespread globally, thanks to humans. "These are mineral-like and they will form a marker layer for all geologic time," Hazen says. "The evidence of these crystalline compounds that never existed before is one line of support for calling the Anthropocene a new geologic time period." Chelsea Whyte ■



RICK WILKING / REUTERS

Who do you think it was?

Exposing cyberattackers can easily backfire

KNOW your enemy, the saying goes. But when it comes to cyberattacks, a game theory model suggests that pointing the finger at perpetrators might not be the best tactic, and could even play into the hands of attackers.

Attributing cyberattacks to their source can be difficult, as was seen last year in the breach of email accounts belonging to members of the US Democratic National Committee (DNC). After investigations by intelligence agencies, the US eventually attributed this attack to Russia.

But naming who's behind an attack may not be helpful if you can't retaliate, says Benjamin Edwards at IBM Research, who led the modelling work.

If someone steals private documents or hacks infrastructure such as power grids or nuclear controls, say, the first problem is working out who it was. To do this, security experts look at the tools used and compare them against those known to be employed by different countries, intelligence agencies or cybercrime groups, like tracing a digital fingerprint.

It's crucial to trace it to the

right people, says Chris Kiekintveld at the University of Texas at El Paso. "You wouldn't want to retaliate against China, for example, for an attack that was actually sponsored by a different country," he says.

If you can identify who attacked you, you can publicly name them. You might also be able to retaliate – but you need a good target and must know your

"Attacking first is the way to go if you don't have much to lose in a counterattack"

enemy's vulnerabilities. If you can't identify the attacker or don't have an appropriate target, you can't respond effectively (*PNAS*, doi.org/b2dw).

Play the theory out and it means that attacking first is the way to go if you don't have much to lose in a counterattack. North Korea, for example, has a lot to gain from hacking enemies, because its cyber infrastructure is limited enough that an adversary doesn't have much of a proportional target to hit back at.

"If there's no effective way to strike back, it'd be embarrassing to blame the perpetrator," says Steven Bellovin at Columbia University in New York.

In some cases, it may even benefit an attacker if you name them, because this could bolster their reputation as a cybersecurity threat. "There's a saying in chess: 'A threat is always stronger than an actual attack,'" says Bellovin. "Once you actually launch the attack, the enemy sees what's coming and can figure out how to respond. If they know you have capabilities but don't know what you're going to do, they have to defend everything."

Edwards and his colleagues use the 2016 DNC email leak as an example of how the blame game can play out.

After investigating, the US eventually responded to public pressure and identified Russia as the attacker. Countermeasures included expelling 35 Russian intelligence operatives living in the US under diplomatic protection. But in a press conference on 15 December 2016, President Barack Obama said: "The idea that somehow public shaming is gonna be effective, I think doesn't read the thought process in Russia very well."

Edwards says this is consistent with the new model. "It was nice to see him indicating that the theoretical predictions this paper makes are things that policy-makers find reasonable," he says.

But the game theory model has limits. Nations take into account more than just a binary judgement of an enemy's weakness, because they must also consider broader political effects.

The issue is further complicated by variation in cyberattack policies around the globe, says Susan Landau at Worcester Polytechnic Institute in Massachusetts. The US, for instance, says it doesn't aim cyberattacks at civilian infrastructure, while some of its adversaries do. Chelsea Whyte ■



RICK FINDLER / BARCROFT MEDIA

Neanderthals still control our genes

Andy Coghlan

THEY may have been extinct for 40,000 years, but Neanderthals are still affecting the illnesses some people develop and how tall they are. This is thanks to the Neanderthal DNA inherited by people outside sub-Saharan Africa from ancestors who mated with our cousins some 50,000 years ago.

Evidence that Neanderthal control of human genes endures comes from an in-depth analysis of DNA from 214 people of European descent in the US. By comparing their DNA with that from Neanderthals – whose genome was sequenced in 2008 – a team led by Joshua Akey at the University of Washington in Seattle identified which Neanderthal gene fragments had survived and were still active in 52 different types of human tissue.

The team found that some people had one human and one Neanderthal copy of the same gene. When comparing these genes, Akey and his team found that a quarter showed differences

in activity between the modern and Neanderthal versions of the gene. More importantly, the researchers could tell which variant had the upper hand.

In one example, Neanderthals may still be protecting some people from developing schizophrenia. A gene called *ADAMTSL3* is a known risk factor for schizophrenia, while also influencing height. But the way the gene is controlled by surviving Neanderthal DNA reduces the risk

"Neanderthal sequences affect how human genes are expressed, including for height and health"

and increases height, the team found. "Strikingly, we find that Neanderthal sequences present in living individuals are not silent remnants of hybridisation that occurred over 50,000 years ago, but have ongoing, widespread and measurable impacts on gene activity," says Akey.

Most genes can generate a variety of different proteins that do different jobs in different

tissues of the body, depending on how sub-units of the protein are assembled. Akey's study shows that the key contemporary impact of the Neanderthal remnants is in dictating which variant of a protein gets produced today.

"The results add to increasing evidence that these effects are often the outcome of changes to the genetic switches," says Tony Capra of Vanderbilt University in Nashville, Tennessee. His own results published last year revealed Neanderthal influences on human disorders, including depression and addiction.

"The implication is that these variants that came into the human gene pool around 50,000 years ago are still affecting human biology," says Sriram Sankararaman at the University of California at Los Angeles. "Neanderthal genes many of us carry in our genomes affect diverse human traits by dictating how genes are regulated."

In brain and testes, however, the influence of our long dead cousins is receding (*Cell*, DOI: 10.1016/j.cell.207.01.038). "The finding that Neanderthal variants tend to have lower activity in brains and testes is intriguing, as it offers hints on which aspects of biology diverged most rapidly between Neanderthals and us," says Sankararaman. ■

Helicopter drone morphs into a plane

IT'S a transforming toy for adults. A shape-shifting drone takes off like a helicopter, then converts into a plane to fly all day on solar power. The drone is designed to provide affordable aerial surveys for farmers, so they can see which spots they need to irrigate or use fertiliser or herbicide on.

Most drones aren't ideal for this because they have short flight times. The Solar Unmanned Air Vehicle: Quad (SUAV:Q), developed by Nikolas Papanikolopoulos at the University of Minnesota in Minneapolis and his team, follows a new approach.

The drone uses vertical take-off and landing (VTOL), but once it is in the air, its powered hinges unfold it into a flat, winged aircraft. The design makes it easier to launch than a fixed-wing drone, and means it can get a stable view during flight of the land below. It morphs back into a quadcopter to land.

"The idea is that anybody can buy this and carry it around in their pickup truck," says Papanikolopoulos.

The craft has a 2.1-metre wingspan so it can carry a multispectral camera for assessing crop health, and weighs just under 4 kilograms. The surface of the wing is covered in solar cells, yielding enough power for continuous flight during the day.

The drone has flown in both of its configurations, and made an in-flight transformation in a wind tunnel. Over the next 6 months, the team will test the transition during real flights.

The device could be helpful to people who oversee large areas of crops, says Ivan Grove at Harper Adams University in Newport, UK. "The current range of VTOLs are mainly the multirotors, which suffer from short flight times in comparison to their fixed-wing counterparts."

Although the transforming drone is aimed at farmers, its long flight time could make it attractive for other uses, such as inspecting infrastructure, forestry and firefighting. David Hambling ■

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Job application tool tackles hiring bias

Matt Reynolds

IF GETTING shortlisted for a job interview seems like a lottery, that's because it often is. Bias can affect the way recruiters view applicants who send in a CV or complete an application form. Behavioural science is at the core of a new system that tries to strip prejudice out of recruitment, so that candidates are judged only on their abilities.

The system, called Applied, was developed by the Behavioural Insights Team, a company set up by the UK government to apply behavioural psychology to government services and policy. It is already being used by the UK civil service, the charity Cancer Research UK and publishing company Penguin, and became commercially available last week.

Fairness in recruitment doesn't just matter to candidates. There is evidence that companies with a truly diverse workforce are likely to perform better. Yet multiple studies suggest that ethnic minority applicants, for example, are less likely to be interviewed or offered jobs than equally

qualified people not from minority backgrounds.

The Applied system forgoes CVs, instead asking candidates to answer five online questions that relate specifically to the job they are applying for. Multiple recruiters then evaluate the replies without knowing which came from which candidate. What's more, each recruiter receives the answers in a different order to minimise the "halo effect": the possibility that one exceptionally good or bad answer

skews how the next is perceived.

The Behavioural Insights Team told *New Scientist* that they tested the system when assessing 700 candidates who had applied for jobs with them. They also asked the candidates to submit CVs to a separate group of recruiters.

Applicants shortlisted by the Applied system came from a wider set of universities and had a broader range of skills between them than those with highly rated CVs, the team found. "Over 50 per cent of the candidates that we hired, we wouldn't have hired if we hadn't used the platform," says Kate Glazebrook, who leads the Applied team.

Glazebrook says that much of the conventional hiring process seems to come down to chance.

In the trial, recruiters who had just read a great CV were more likely to rate the next one they read more harshly, and the ratings for the first few CVs reviewed were inconsistent as the recruiter tried to work out what a good application looked like.

But anonymised applications aren't a magic bullet against workplace discrimination, says Rachel Marangozov at the Institute for Employment Studies in Brighton, UK. "It might just postpone discrimination until the interview stage," she says.

It may also not lead to more diverse candidates being selected. A study in France in 2010 found that when employers opted to have applicants' CVs stripped of details such as name, gender and nationality, they were actually less likely to hire minority candidates. The researchers concluded that this may have been because the companies that volunteered for the study were already more likely to hire minority candidates, and anonymising CVs made it harder for them to take background into account.

Glazebrook says that Applied does not necessarily aim to increase workplace diversity. "It's about hiring the best person irrespective of their background," she says. "We've been quite clear in the platform that we don't allow for positive discrimination at all among reviewers." ■



It's not the suit that counts

Each loaf of bread produces half a kilo of CO₂

GIVING you your daily bread is costly for the climate. The equivalent of half a kilogram of carbon dioxide goes into the atmosphere for every loaf of bread produced in the UK, according to the best study on the subject yet.

This suggests that making the bread eaten in the UK leads to greenhouse gas production equal to half a per cent of the nation's carbon

emissions. The finding also highlights the need to tackle global emissions from farming, which produces a third of all greenhouse gases.

In the case of bread, the main contributor is the nitrogen fertiliser used to grow wheat: making and using fertiliser creates 40 per cent of the emissions. "The 40 per cent figure was quite a shock to us," says Liam Goucher at the University of Sheffield in the UK, whose team worked with farmers and an industrial bakery to directly measure what goes into producing a wholemeal loaf.

While several other teams have

calculated the emissions associated with bread-making, those studies relied more heavily on estimates than direct measurements.

The new study found that two-thirds of fertiliser emissions come from its manufacture, a high-temperature process usually reliant on natural gas (*Nature Plants*, DOI: 10.1038/nplants.2017.12).

Fertiliser can be made by using

"The biggest part of carbon emissions from making bread comes from fertiliser used in wheat farming"

renewable energy instead. However, as this process is much more expensive, there is no financial incentive to switch.

The other third of fertiliser emissions are due to nitrous oxide. Bacteria in soil convert a little of the nitrogen in fertilisers into this highly potent greenhouse gas and release it into the air.

While it might seem the way to reduce fertiliser emissions is to switch to organic farming, other studies have found that organic wheat is just as bad if not worse for greenhouse gas emissions. Michael Le Page ■

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Quite an impact

Greatest asteroid damage from wind

Leah Crane

WIND kills. Most casualties from an asteroid impact won't come from the impact itself. The resulting wind, pressure spikes and heat are far more dangerous, no matter where the asteroid hits.

Clemens Rumpf at the University of Southampton, UK, and his colleagues have calculated the mortality risk, should an asteroid hit a residential area. They considered asteroids that burn up completely before impact, those that hit the ground and those that strike in water. Surprisingly, the airborne side effects were the ones that cost the most lives.

As an asteroid hurtles towards the ground, it deposits a huge amount of energy in the atmosphere, resulting in a powerful shock wave, tornado-like winds and a plume of fire trailing behind it. When it crashes down, it forms a crater, shaking the ground and hurling debris into the air.

If the asteroid hits water, which is twice as likely as hitting land, it would create a tsunami, with waves reaching dozens of metres

high. The farther from shore the impact is, the deeper the water and the taller the waves.

In the past, researchers have shown that tsunamis pose the greatest risks from an asteroid impact, but the events are hard to model. Rumpf's team has worked out that the continental shelf protects the shore by dissipating waves both at its steep edge and over its gentle beachward slope.

"What sets tsunamis apart is that they're really the most far-

"In an impact, wind and surging temperatures are joined by pressure waves, which can rupture organs"

reaching effect of all the impact effects," says Rumpf. A pressure wave or heat plume can't travel very far, and craters only form right at the impact site, but tsunamis can traverse hundreds of kilometres of ocean to hit coastal communities.

A tsunami caused by the impact of a 200-metre-wide asteroid 130 kilometres off the coast of Rio de Janeiro, for example, could

cause more than 50,000 deaths, with 75 per cent of those being directly caused by the tsunami and the rest due to high winds.

But an asteroid over or in a city would kill millions. Most deaths would be due to wind as well, even if the asteroid did crash to ground instead of exploding in the air.

For an airburst, about 15 per cent of casualties would come from heat. In a direct impact, the effects of gusting wind and surging temperatures are joined by pressure waves, which can rupture internal organs.

Only about 3 per cent of casualties would be caused by the actual impact or the earthquakes and debris that result, says the team (arxiv.org/abs/1702.05798). The group plans to discuss the results with disaster managers to come up with suggestions for preparedness.

Luckily, large asteroids don't hit Earth often: an impact by a 200-metre asteroid is expected only once every 40,000 years. And there are lots of projects dedicated to planetary defence.

"We are in the business of detecting asteroids well in advance of an impact, so this kind of work is only really important if we totally fail to do our jobs," says Erik Christensen, director of the Catalina Sky Survey at the University of Arizona, Tucson. ■

Mental tests may predict top sporting skills

HOW can you predict who will make a great athlete? Testing their executive functioning may be the answer.

Executive functioning describes unconscious mental abilities, such as working memory, which helps handle information to make decisions, and attentional control, which is our ability to choose what to ignore.

Torbjörn Vestberg at the Karolinska Institute in Stockholm, Sweden, and his team have assessed these abilities in 49 players under the age of 20 at an elite soccer academy in Sweden. The tests included the trail making test, which measures the brain's processing speed, visual search speed and mental flexibility, by getting people to draw lines between ascending numbers spread randomly on a page.

Even after controlling for factors that could affect performance on the field, the athletes who had higher executive function scores netted more goals over a two-year period (*PLoS One*, doi.org/bz95). Vestberg says such skills match up with what is required of soccer players and other athletes. "When you're more successful in soccer, you have cognitive flexibility, you can shift focus, you can suppress behaviour, you can be creative and find solutions very fast," he says.

It makes sense for athletes competing at the highest level to have these enhanced mental abilities, says Jocelyn Faubert at the University of Montreal, Canada. "It's on-the-fly decision-making," he says. "Reading all the input, taking all that in and acting on it does require some fundamental cognitive capacities."

It isn't clear if this cognitive skill in athletes is innate, or if it is a result of training, says Faubert. But the research helps tease out what makes elite athletes special. Vestberg says such tests might help coaches identify late bloomers - youngsters who start off smaller physically, but who have the cognitive profile to be successful athletes later on. Nicole Wetsman ■



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IN BRIEF

JOHN CAREY/GETTY



Try 10 fruit and veg a day to keep the doctor away

PASS the fruit bowl. Five a day just doesn't cut it any more - we should be eating 10 portions of fruit and vegetables a day to reduce our chances of dying from a heart attack or cancer.

That's according to a review of 95 studies looking at the relationship between diet and health by Dagfinn Aune of Imperial College London and colleagues. "Five a day is good, but more is even better," says Aune.

Official advice in the UK is to eat five portions of fruit and veg a day. A portion is about 80 grams - an apple, two tangerines or three heaped tablespoons of peas, say.

In the latest review, people who ate 10 portions a day were nearly a third less likely to die during the course of the studies than those who ate none. The studies followed people for between three and 30 years. Most benefits stemmed from reductions in the rates of heart disease and cancer, the commonest causes of death in Western countries (*International Journal of Epidemiology*, doi.org/bz94).

Risk of dying from cancer, for instance, fell as people ate more cruciferous vegetables, such as broccoli, although this finding came from only a few studies that investigated the benefits of particular types of produce.

The biggest health benefits were seen when people increased intake from zero to five a day, but people shouldn't stop there, says Aune.

Smoking makes you drink more coffee

FANCY a coffee after a cigarette? Smoking makes you drink more caffeinated drinks – possibly by changing your metabolism so that you break down caffeine quicker, pushing you to drink more to get the same hit.

Marcus Munafò at the University of Bristol, UK, and his colleagues analysed data on the smoking and drinking habits of about 250,000 people from the UK, Norway and

Denmark. They were particularly interested in people who had inherited a variant of a gene that predisposes them to become heavier smokers.

The team found that people who had the gene variant also consumed more coffee – but only if they smoked (*bioRxiv*, doi.org/bz96). The gene variant codes for a nicotine receptor, which is not known to directly interact with

caffeine. Together, the results suggest that cigarette smoking increases caffeine consumption, and not the other way around.

There's a chance that smoking and caffeine consumption are linked through habit, but Munafò thinks that nicotine in cigarettes might also make smokers metabolise caffeine more quickly. If that is the case, they might need to consume more caffeine to get the same effects that a non-smoker would experience.

Augmented reality curbs road rage

YOU'RE driving along and someone cuts you up. Just as you're about to honk your horn, a virtual note appears on your windscreens: "Rushing to the hospital". Your anger dissipates.

Chao Wang and colleagues at Eindhoven University of Technology in the Netherlands developed the augmented reality system to reduce road rage by helping drivers communicate. The prototype projects data from a smartphone app onto a transparent display. It flashes up messages from other drivers using the system when the phone camera spots a sticker on their rear window.

In a driving simulator trial, people were more empathetic toward erratic drivers if they saw AR signs explaining their situation. The team will present the work at the Intelligent User Interfaces meeting in Cyprus later this month.

Musical caterpillars 'drum' with anus

ONE tiny caterpillar is a musical maestro among insects. It turns out that masked birch caterpillars (*Drepana arcuata*) use many bits of their body, including anal "oars", to make sounds.

"They shake their bodies, drum and scrape their mouthparts, and drag specialised anal 'oars' against the leaf surface to create bizarre signals," says Jayne Yack at Carleton University in Ottawa, Canada.

She thinks they may do this to invite other caterpillars to areas with food to build silken shelters together (*Behavioral Ecology and Sociobiology*, doi.org/b2ch). "I've been studying insect sounds for more than 30 years, and I've never seen one insect species produce such a diversity of signal types."

Bees learn to play golf to get snacks

IT'S a hole-in-one! Bumblebees have learned to push a ball into a hole to get a reward, stretching what small-brained creatures were thought capable of.

Previous studies showed that bees could do smart things to objects directly attached to a food reward, such as pulling a string to get at food. Olli Loukola at Queen Mary University of London and his team decided the next challenge was to get bees to learn to move an object not attached to a reward.

They built a circular platform with a small hole in the centre filled with sugar solution, into which bees had to move a ball to get a reward. A researcher showed them how to do this by using a plastic bee on a stick to push the ball.

The bees did learn, and even minimised the effort needed by choosing the ball closest to the hole (*Science*, doi.org/bz98).

"They don't just blindly copy the demonstrator; they can improve on what they learned," says Loukola. He thinks this ability to copy and refine what they observe could help the bees forage successfully in changing natural environments.

Loukola also thinks the behaviour fulfils the criteria of tool use - normally regarded as the preserve of only a few particularly intelligent animals, such as primates and crows.



LIDA LOUKOLA

Deep learning smashes pro players at their own video game

AI has taken on professional players of a cult Nintendo game – and won.

A team led by Vlad Firoiu at Massachusetts Institute of Technology trained the AI to play *Super Smash Bros. Melee* using deep learning algorithms, and pitched it against 10 highly ranked players. The AI came out on top against every one of them.

In the game, players aim to knock out classic characters like Super Mario and Zelda by sending them out of bounds. It may not be as complex as strategy games like

Go, which Google DeepMind's AlphaGo mastered in 2016, but Firoiu says it poses a different challenge for AI because you can't plan many moves in advance. *Super Smash Bros. Melee* is also multiplayer, unlike many video games AI has conquered, such as *Pac-Man* and *Space Invaders*.

The researchers used a technique called reinforcement learning, letting their system find out the best moves by playing first against the game's built-in AI, and then against itself. That done, they asked pro players at

Super Smash Bros. tournaments to try to defeat it.

The AI won more fights than it lost against each of the 10 players it fought, who ranked from 16th to 70th in the world (arxiv.org/abs/1702.06230). "After a couple of hours the AI was good enough to beat the in-game AI, and after a couple of weeks it could beat the top-ranking humans," says Firoiu.

However, the AI has a fatal flaw that these players didn't notice. If an opponent crouched at the side of the stage, it didn't know what to do – and knocked itself out.

Voyager 1 snapped Enceladus plumes

WE COULD have spotted the icy plumes of Saturn's frozen moon Enceladus 25 years earlier than we did, if only we had known to look.

Plumes were first observed erupting from Enceladus's south pole by NASA's Cassini spacecraft in 2005. Further observations suggest that the moon hosts a subsurface sea that could be one of the best places in the solar system to look for life.

Now Ted Stryk, a space image-processing enthusiast from Tennessee, believes he has made a "pre-discovery" of those plumes in archive image data from the Voyager 1 probe, which raced past the Saturn system in 1980.

Stryk processed Voyager 1 images that are publicly available from NASA's online Planetary Data System to reveal a faint protrusion emanating from the moon's southern hemisphere.

The work will be published at the Lunar and Planetary Science Conference in Texas next month.

If we confirm the plumes in another archival image, it could tell us how long they have been active, says Andrew Coates, a Cassini scientist at University College London's Mullard Space Science Laboratory.



GEORGE ROSE/GETTY

Snow to melt slower as world warms

AS GLOBAL temperatures rise, snow will melt more slowly. Yes, you read that right – more slowly.

Warmer global temperatures will lead to shallower snowpack in many mountainous areas, says Keith Musselman, a hydrologist at the National Center for Atmospheric Research in Boulder, Colorado.

That thinner layer of snow will be less likely to last into the late spring and early summer, when melting rates are highest. Instead, it will melt away throughout the winter and early spring, when nights are cooler and there is less direct sunlight,

releasing just a trickle of water instead of a gush. So, it melts earlier but at a slower rate.

"The more you think about it, it becomes one of those 'aha' stories," says Musselman, who used historical snowpack measurements and computer models to predict how the melting rate will change by the end of the century (*Nature Climate Change*, DOI: 10.1038/NCLIMATE3225).

A slower melting rate will reduce water availability both for human consumption and for ecosystems that rely on snowmelt, such as the mountains in the western US.

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Microbes on the market

A legal loophole means some promising drugs are already available as food or cosmetics. Is that a good idea, asks **Jessica Hamzelou**

FOR the last decade, we've been promised that one day, we'll be able to mine and modify our microbiomes – the bacteria that live in and on our bodies – to tackle diseases and stay healthy. So far little in the way of practical applications has emerged. This year is different, as attendees at the Human Microbiome Congress in San Diego heard.

A key theme animating the recent conference was the explosion of drugs targeting the microbiome: at least 70 start-ups and institutes are now competing to get the first drugs to market. Pharmaceutical companies are heavily represented – including Bristol-Myers Squibb, Pfizer and Merck – but many other players are supported by private investment and even crowdfunding initiatives. "Collectively, these companies have well over a billion dollars of investment," says Dirk Gevers at the Janssen Human Microbiome Institute in Spring House, Pennsylvania.

As these potential drugs make

their way through clinical trials, early results are promising, but they won't be on the market for three to five years.

However, several of the drugs now in various stages of human trials are already available, or soon will be, thanks to a regulatory loophole that allows them to be sold as cosmetics or food supplements. As long as

"One skin spray on the market alleviated high blood pressure, allergies and migraine"

they make no medical claims before trials conclude, such products are not subject to the same regulations as a medicine.

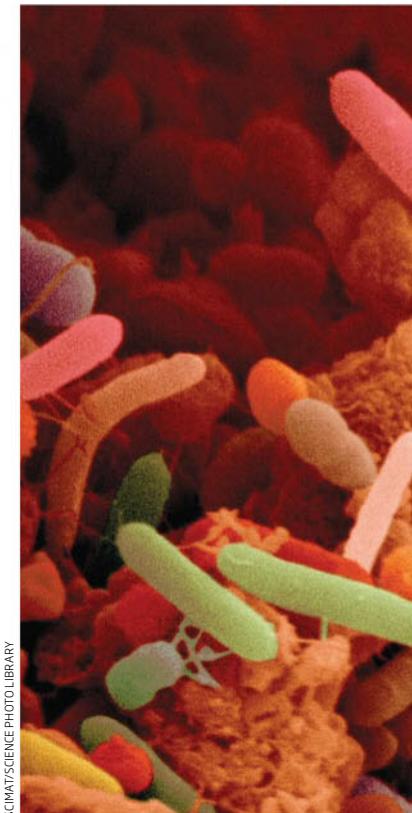
The people buying them are discovering that they can have dramatic health effects, but some researchers are worried. "With all the hype about the wonders of microbiome-based medicines, the market is ripe for the picking," says Eugene Chang at the University of Chicago in Illinois. Are these products the real deal?

Some of the effects certainly seem to be. One UK-based company, OptiBiotix, sells a range of snack bars meant to control glucose metabolism. Their customers claim to have lost weight and feel less hungry. Last week, the company released results on early research in 50 people whose cholesterol levels had dropped after taking this treatment for 12 weeks.

Later this year, another food supplement, a smoothie mix sachet developed by Microbiome Therapeutics will be available for purchase. The US company recently concluded a small pilot study of the compound, finding that it helped to regulate the blood sugar of volunteers who had diabetes and were pre-diabetic (see chart, below).

The gut microbiome is not the only target. Manipulating the bacteria that cover the skin can also have powerful effects.

In the course of testing its bacterial face spray for acne, San Francisco start-up AOBiome discovered that the spray also



SCINIAS/SCIENCE PHOTO LIBRARY

brought down volunteers' blood pressure. To investigate this effect further, the company have begun a separate trial.

The 50,000 customers who have bought the spray as a cosmetic have also reported other effects. Some noticed a reduction in migraines, leading to yet a third trial now in early stages. "We aren't making any claims, but people are already spraying this stuff everywhere," says Larry Weiss, the CEO of AOBiome. Still others reported reduced allergies and yeast infections. "These are case reports, and not conclusive," he says, "but they are an important part of medical discovery."

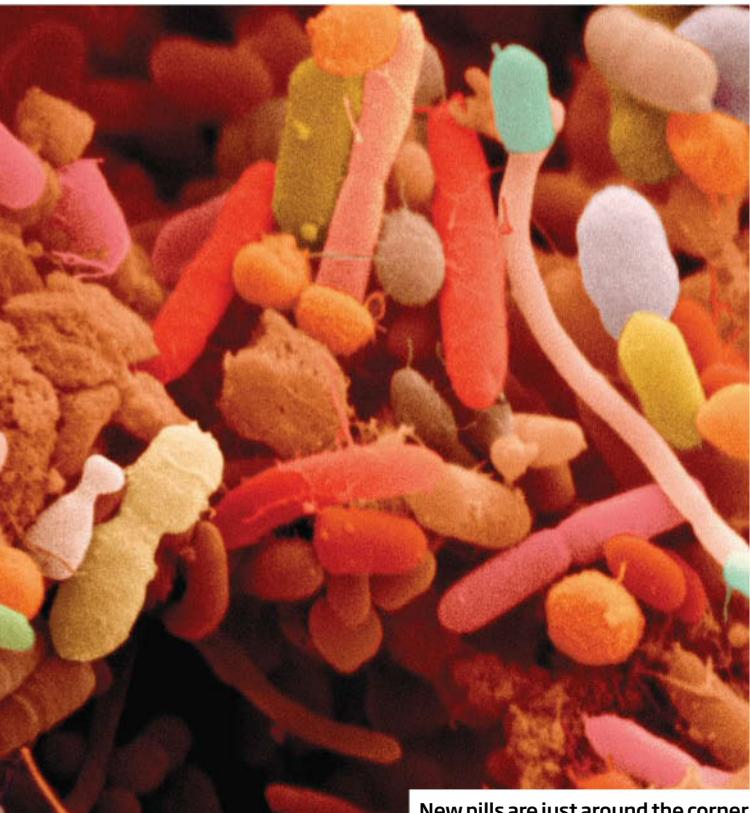
Last resort

For some, these products are the only things that have helped their conditions (see "Bacteria in a bottle cured my acne", right). But it raises the question: is it wise to use these before

TESTING, TESTING...

The next generation of products will manipulate or add to your own microbiome. Some can be bought already

PRODUCT	COMPANY	AVAILABLE TO BUY?	IN TRIALS FOR...
MOTHER DIRT bacterial mist spray	AOBiome	Yes, if you live in the US	Acne (phase 2) Hypertension (phase 2) Allergic rhinitis (phase 1) Migraine (pre-clinical)
NM504 smoothie mix	Microbiome Therapeutics	Will be launched in August	Diabetes and pre-diabetes (pilot study)
SLIMBIOME snacks and shakes	OptiBiotix	Can be bought online	High cholesterol (pilot study)
RP-G28 compound to stimulate bacteria growth	Ritter	No	Lactose intolerance (phase 2)
LACTIN V vaginal bacteria powder	Osel Inc	No	Bacterial vaginosis (phase 2) Recurrent urinary tract infections (phase 2)



New pills are just around the corner

trials have concluded?

The only insights into this question come from the previous generations of microbial treatments: probiotics and prebiotics backed by little evidence, and, at the other extreme, faecal transplants.

The latter is the only one backed by evidence, but squirting someone else's faeces inside you isn't a decision to be taken lightly. In the US, this is only approved to treat *Clostridium difficile* – a hospital-acquired infection that can strike after antibiotics strip beneficial bacteria from the gut. A faecal transplant from a healthy donor is thought to restore the natural balance, reflected in the 90 per cent cure rate.

However, it's a blunderbuss approach. Faeces can teem with millions of bacterial strains as well as viruses and fungi. Some of these may be responsible for surprising and sometimes unpleasant consequences of faecal transplants – including

obesity. These have led to calls for regulation in countries with fewer restrictions. "I think sooner or later we're going to start seeing negative consequences of faecal transplants," says Chang.

This explains why many of the drugs in trials are attempts to create faecal transplants without, well, the faeces. The key to turning this into a standardised and predictable treatment is finding and isolating the specific "healthy" bacteria that should repopulate the gut. Emma Allen-Vercoe at the University of Guelph in Ontario, Canada, is developing a combination of 40 bacterial strains that can be taken as an oral capsule. "We don't rely on a donor at all," she says.

Drugs for *C. difficile* are the first port of call. But for less dire conditions, there are other

"If you see health benefits, you don't have to understand the whole system to manipulate it"

approaches to manipulating the microbiome. Instead of bacteria, some of the drugs contain ingredients, such as certain kinds of fibre, which nurture the growth of the "friendly" bacteria present in your gut. Pharmaceutical firm Ritter is using this approach to boost the growth of bacteria that ferment lactose, and found this made it easier for lactose-intolerant volunteers to digest dairy foods. The same approach underpins the snack bar and the shake that are now on the market.

Déjà vu?

Stripped of the unpredictable and unknown denizens of faecal transplants, then, these products may be less likely to cause similar unintended consequences. But the other risk is that the stuff simply won't work. This has been a frequent criticism of supermarket probiotics, bacteria-rich capsules and yogurt supported by very little evidence. Because they are marketed as nutraceuticals, their makers evade regulatory scrutiny even as they make vague claims about health. "Proof of these claims is often based on in-house testing which is frequently questionable or flawed," says Chang.

Although their trials are small, AOBIOME's work is based on a lot of pre-clinical work, Weiss says. He says the company works closely with the Food and Drug Administration, which is also overseeing and guiding similar drugs to the more advanced clinical trials.

The majority of microbiome drugs are not on the market, but their progress is swift. "This field is moving faster than any other field we've seen," says Gevers.

Even self-confessed sceptics like Chang are optimistic that this next wave of microbiome drugs represents the future of medicine. If the products being sold as cosmetics and food supplements clear all the proper hurdles, they will join the new pantheon. ■

CASE STUDY

BACTERIA IN A BOTTLE CURED MY ACNE

"I've had acne since I was about 9 years old," says blogger Sabrina Zimmerman, who lives in New York state. "I was bullied and made fun of."

As she got older, Zimmerman developed cystic acne – which causes painful blemishes that are more deeply embedded in the skin, leaving deep scars.

Zimmerman tried "everything on the market" to get rid of her acne. "I saw dermatologist after dermatologist," she says. But nothing worked.

Last year, Zimmerman heard about a line of products that contain bacteria from soil. The products, marketed under the name Mother Dirt by a firm called AOBIOME, have cleared safety stages to move into more advanced clinical trials for skin disorders, high blood pressure and migraine – but for the time being they can be purchased as cosmetics (see main story).

SPRAY AND HEAL

One of these products delivers bacteria in the form of a mist spray. Since the end of last summer, Zimmerman has been spraying the product all over her body every morning, and spraying her face before bed. "My skin started to heal," she says.

After decades of skin problems, Zimmerman's acne has cleared up. "I still get the occasional hormonal acne, but it's nothing like the continual breakouts I was having before," she says.

Zimmerman also uses the spray alongside her deodorant "to keep odour away". And she has noticed another, more surprising outcome since using the spray all over her body. "I used to have chronic yeast infections," she says. "After using it in that area, I don't get them any more."

While the product is in clinical trials, the company can't make any claims about its effectiveness. But around 50,000 of the sprays have been sold to date. Some users are reporting other benefits, which have led to new investigatory trials for the drug.

No way back for Pluto

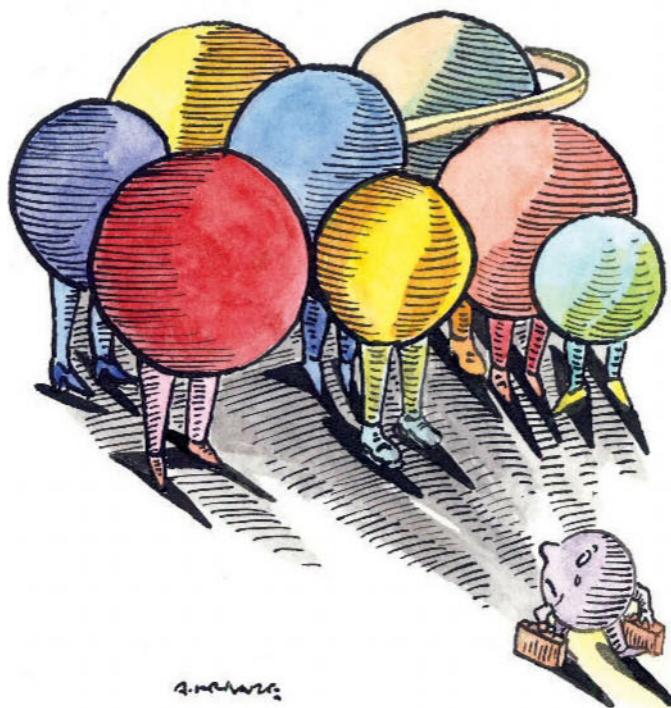
Pluto is still an ex-planet, despite what its most ardent fans claim, says astronomer **Michael Brown**

A SMALL but vocal group led by Alan Stern, the scientist in charge of NASA's New Horizons mission, is trying to reverse the decision made over a decade ago to remove Pluto's planet status.

Why? Has anything changed? No. The proposal is essentially the same case made for keeping its status that was rejected in 2006.

The problem is that the proposal would mean defining all round objects smaller than stars as planets. Pluto would be back. But it would bring a lot of baggage with it. Like our own moon.

Today, most of us would say the moon is not a planet, but 500 years ago, when people thought the moon and the sun revolved around Earth, they were just two of seven "planets", along with Mercury, Venus, Mars, Jupiter and Saturn. With the Copernican revolution in the 16th century, the definition of planet changed.



They were now the things going around the sun. The moon was the one thing going around Earth. Then the moons of Jupiter and Saturn were found. We were beginning to learn about the real solar system. Uranus became the seventh planet in 1781.

In 1801 the first asteroids were found between Mars and Jupiter. They, too, were initially called planets. But the discovery of Neptune as the eighth planet in 1846 coupled with the discovery of more asteroids in the Mars-Jupiter region was a reminder that, while many objects orbit the sun, there are only a few dominant ones. Asteroids were reclassified as minor planets.

Finally came Pluto, further out still, in 1930. It was hailed as the ninth planet. But in 1992 many asteroid-like bodies began to be found in those distant regions. In 2005, I found Eris, one such object

At a crossroads

Car-makers face a dilemma over the best route to a self-driving future, says **Jamais Cascio**

DRIVING can be tedious, and the journey doubly so for a passenger. Now imagine the worst of both worlds: a driver having to focus on dull traffic while simply being a passenger most of the time. That is exactly what the next step in autonomous vehicles promises.

The US National Highway Traffic Safety Administration

uses a six-level scheme to grade autonomy. Level 0 is all human. Level 1 includes basic systems like adaptive cruise control. Level 2 allows for simple steering autonomy with constant driver oversight (as with Tesla's Autopilot).

Level 3 allows the driver to safely turn attention away on

some road types, but to be ready to take over – and it's what is up next for commercially available autonomous cars. Audi is poised to launch one by 2018, with Nissan, Honda and Kia to follow.

However, Ford has cast doubt on the wisdom of this road map. In tests of level 3 systems, it has found that drivers lose "situational awareness", sometimes falling asleep. The problem persists even with buzzers, vibrating seats and a

"Waymo CEO John Krafcik goes so far as to wonder whether level 3 autonomy may turn out to be a myth"

second engineer to watch the first.

As a result, Ford technical lead Raj Nair has restated the company's desire to skip level 3. It aims to make fully autonomous cars by 2021, without pedals or steering wheels, for use within a predefined area: level 4 autonomy. The intent is to create a vehicle for ride-sharing or ride-hailing. Passengers would be free to chat, use phones or nap without worrying about taking control... because they can't take control.

Skipping the possible pitfalls of level 3 sounds tempting. But equally, as car-makers race to get models out and capture consumer interest, this could prove too big a

that was more massive than Pluto, and the debate over how to classify these bodies came to a head.

As with nearer asteroids a century before, it became clear that good classification required separating the true planets from the uncountable tiny objects. Pluto and Eris belong to this new population of small objects beyond Neptune. This distinction is critical for understanding how our solar system came to be and why it is the way it is.

If all round things are planets regardless of where they are, then the moon – round and five times as massive as Pluto – is our closest planetary neighbour.

You can't have a scientifically consistent definition of "planet" including Pluto but not the moon. It's hard to imagine much support for such an odd proposition.

The New Horizons fly-by showed that Pluto is fascinating and worth studying. Instead of mistaking "fascinating" for "must be a planet", let's instead celebrate what this little world tells us about how much there still is to learn about our solar system. ■

Michael Brown is professor of planetary astronomy at the California Institute of Technology and author of *How I Killed Pluto and Why It Had It Coming* (Spiegel & Grau)

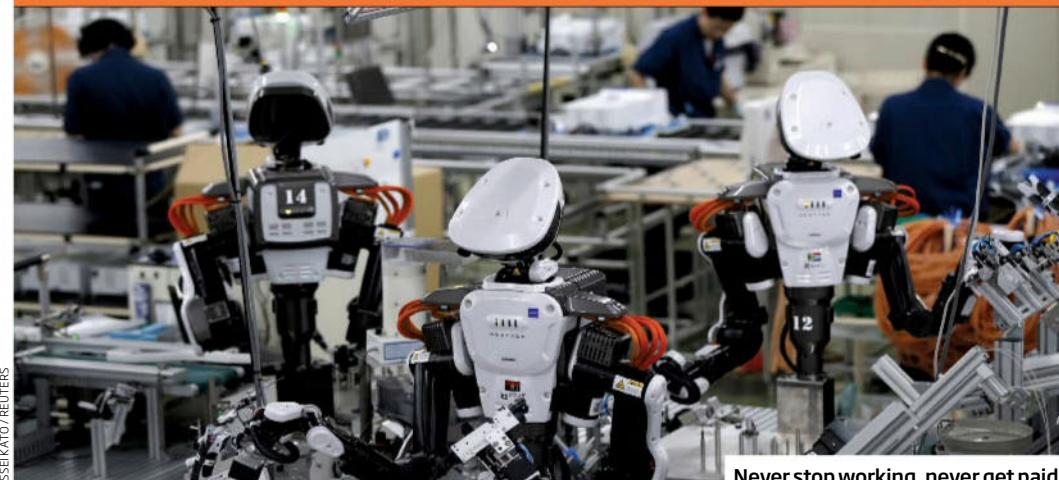
step in a short time. For example, will voice interfaces really be good enough in just four years to permit cars without controls?

There are hazards ahead for both camps. Ford and Google's Waymo may soon be asking the public to put their total trust in these new technologies. That's a big leap and a big gamble.

Reacting to Ford's sleeping test drivers, Waymo CEO John Krafcik has gone so far as to wonder whether level 3 autonomy "may turn out to be a myth". We are about to find out. ■

Jamais Cascio is a distinguished fellow at the Institute for the Future, California

INSIGHT Automation



ISEKI KATO/REUTERS

Never stop working, never get paid

A robot tax is only the beginning

Sumit Paul-Choudhury

IS IT time we started taxing robots? Not the robots themselves, of course – their wages remain stuck at zero – but employers who would automate human jobs out of existence.

Bill Gates thinks we should: in a recent interview, he argued that we should raise the same amount of money by taxing robots as we would lose in payroll taxes from the humans they supplant. That money could be directed towards more human-dependent jobs, such as caring for the young, old and sick. His remarks came just a day after EU legislators rejected just such a proposal, perhaps swayed by the robotics industry's claims that it would slow innovation and ultimately damage the economy.

Automation is shaping up to be the biggest challenge to employment in the 21st century. Whatever Donald Trump may think, the trend to ship jobs overseas is dissipating, while immigrants tend to fill gaps in the labour market rather than oust native workers. According to one study, far more of these job losses are attributable to automation than outsourcing.

That will only get worse as machines become ever more capable of doing human jobs – not just those involving brute labour, but ones involving thinking, too.

Those who back the robot revolution often point out that previous upheavals have always created new kinds of jobs to replace the ones that have gone extinct. However, one important pressure valve might not work this time. Previously, when automation hit one sector, employees could decamp to other industries. But the sweep of machine learning means that many sectors are automating simultaneously.

"Maybe it's not about how many jobs are left after the robots have had their pick, but what kinds"

So maybe it's not about how many jobs are left after the machines are done taking their pick, but which ones.

The evidence so far suggests they might not be very satisfying. For example, we have seen the rise of the "gig economy", in which algorithms direct low-skilled human workers. While this is an employer's dream, it is

frequently an insecure, unfulfilling and sometimes exploitative grind for workers.

What of those jobs that don't yet exist? So far we have only the germs of what these might be. Perhaps augmented reality could deliver expert systems that could be used by staff who no longer need to have years of training. However, the laws of economics imply that this will lessen the wages these jobs command.

If you want to stop this, it's the employers you need to convince, not the people making the technology. Employers have huge incentives to replace all-too-human workers with machines that never stop working and never get paid.

A robot tax might help raise funds to reorient education and training towards the lucrative jobs that remain. Another possibility is the much-discussed proposal to introduce a basic minimum income to take the sting out of joblessness. A more business-friendly middle ground might be for governments to subsidise reductions in working hours, an approach that has fended off labour crises before.

A robot tax, provided it is properly designed, might encourage companies to look for ways to use automation that are both socially and economically advantageous. Properly designed tax breaks for companies that embrace retraining and upskilling workers might help too. It's always better to wield both carrot and stick. ■

APERTURE





Blast off

IF YOU'RE looking into the darkest cosmic recesses, you want the sharpest vision possible. For workers at the Hobby-Eberly telescope in western Texas, this means a ritual repeated every two days: blasting the telescope's primary mirror with dry ice. The solid carbon dioxide dislodges dust then turns to gas, leaving no residue.

First opened in 1996, the Hobby-Eberly is one of the largest optical telescopes in the world. The 91 hexagonal segments of the primary mirror cover almost 78 square metres, and the entire apparatus swivels to cover four-fifths of some of the darkest skies in the continental US.

The telescope is now back in service after a major overhaul. From early 2018, the perfectly buffed mirror will collect light from some 800,000 galaxies that are 11 billion light years away, providing a comprehensive map of the universe when it was less than half its current age.

The aim is to help pin down the nature of dark energy. The discovery in the late 1990s that the universe's expansion is accelerating shocked astronomers. Dark energy is what we call whatever is driving that acceleration, and it seems to make up almost 70 per cent of everything in the current universe. But what is it? How has its influence changed over time? The Hobby-Eberly's snapshot of the past should help us find answers - and perhaps solve other cosmic mysteries along the way (see "Universal (un)truths", page 28).

Richard Webb



Photographer

Enrico Sacchetti



Universal (un)truths

The cosmos is as it is – but what if it isn't?
**Stuart Clark explores five celestial impossibilities
 that might just be true**

1. WHAT IF...

THE SPEED OF LIGHT WERE INFINITE?

The speed of light in a vacuum is the ultimate cosmic speed limit. Just getting close to it causes problems: the weird distortions of Einstein's relativity kick in, so time slows down, lengths go up, masses balloon and everything you thought was fixed changes. Only things that have no mass in the first place can reach light speed – photons of light being the classic example. Absolutely nothing can exceed this cosmic max.

We have known about the special nature of light speed since an experiment by US physicists Albert Michelson and Edward Morley in the 1880s. They set two beams of light racing off, one parallel and one at right angles to the direction of Earth's rotation, assuming the different relative motions would mean the light beams would travel at different speeds – only to find the speed was always the same.

Light's constant, finite speed is a brake on our ambitions of interstellar colonisation. Our galaxy is 100,000 light years across, and it is more than four years' light travelling time even to Proxima Centauri, the closest star to the sun and home, possibly, to a habitable planet rather like Earth.

Then again, if the speed of light were

infinite, massless particles and the information they carry would move from A to B instantaneously, cause would sit on top of effect and everything would happen at once. The universe would have no history and no future, and time as we understand it would disappear. We wouldn't like a universe like that.

But don't put the brakes on just yet. The fact is, a larger light speed would solve one of the biggest problems in cosmology: that the universe's temperature is more or less the same everywhere, even though there hasn't been enough time since the big bang for this thermal equalisation to have taken place (see "Expanding our horizons", page 30).

Standard cosmology solves this problem with inflation, a period in the very early universe when space itself suddenly inflated faster than light speed (something Einstein's relativity does allow), carrying an equalised temperature to far-flung climes. But no one can find a plausible way for space to behave like this. Models of inflation have to be made flexible so they can retroactively fit just about any observation thrown at them.

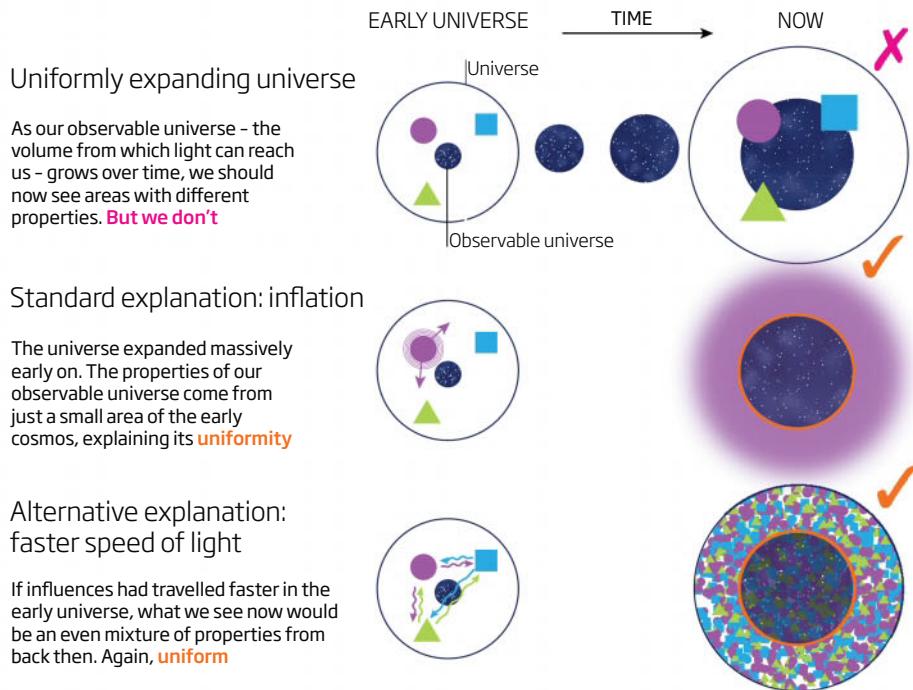
You could achieve the same effect as inflation, however, if cosmic light speed started out infinite (or at least a lot larger) at the big bang and has been getting slower ever since as space has expanded. Initially, the speed fell precipitously. These days, it creeps downwards imperceptibly, explaining why we measure it as a constant. ➤

That sounds wacky, but last year Niayesh Afshordi at the University of Waterloo, Canada, and João Magueijo of Imperial College London proposed ways to test for a variable light speed in galaxy surveys or in fluctuations of the cosmic microwave background, the leftover radiation from the big bang. “The idea that the speed of light could be variable was radical when first proposed, but with a numerical prediction, it becomes something physicists can actually test,” says Magueijo. “If true, it would mean that the laws of nature were not always the same as they are today.”

And we should soon have answers. The HETDEX experiment at the recently upgraded Hobby-Eberly Telescope in Fort Davis, Texas, should next year start to provide data on the distribution of distant galaxies (see Aperture, page 26), as could the Dark Energy Spectroscopic Instrument experiment under construction at the Kitt Peak National Observatory in Arizona, which is due to start taking readings in 2018. Failing that, the next-generation CMB-S4 experiment should scrutinise the microwave background to the required accuracy. This alternative universe might not be too alternative at all.

Expanding our horizons

In the early universe, different areas had different properties – and that should have become apparent to us over time. But in fact we see a **uniform** cosmos. Why should that be?



2. WHAT IF...

QUANTUM WEIRDNESS WERE WEIRDER?

Imagine a world where, if you and I had once met, my missing the bus to work would automatically make you late too. Or where, if I put on odd socks, yours would be odd too. A great excuse, maybe – but also deeply weird.

The classical world we live in isn’t like that. I do X and Y happens, and what Z is doing over there generally has little influence on that. But these clear relationships disappear when we enter the quantum world, the world of subatomic particles that are the building blocks of the universe – and encounter the phenomenon of entanglement.

Described by Einstein in 1935, this is a kind of particle telepathy that defies complete characterisation even today. Particles can become entangled when they interact, and once they do, no matter how far apart they are, measuring the properties of one automatically fixes the properties of the other – changes its socks, as it were.

Einstein decried this “spooky action at a distance”, yet many experiments have shown it is an essential ingredient of our world. “Without quantum entanglement, we could not have quantum theory as we know it, and quantum theory is the basis of chemistry, our semiconductor industry, even life,” says Caslav Brukner of the Institute for Quantum Optics and Quantum Information in Vienna, Austria.

But here’s the really weird thing. There’s nothing stopping the quantum world having different levels of underlying correlation – largely uncorrelated worlds are possible

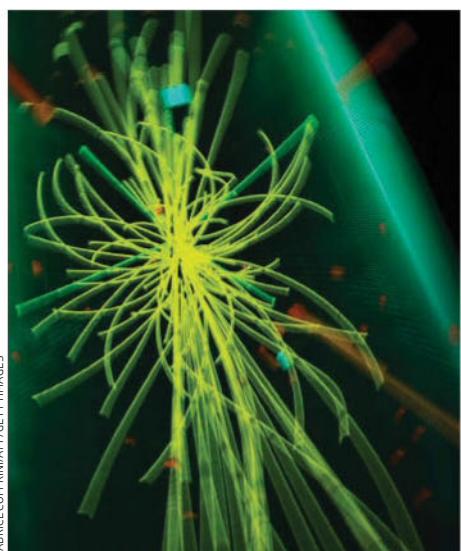
within the broad sweep of the theory, as are ones that are far more connected. But only a universe with the exact level of weirdness that corresponds to entanglement produces the rich tapestry of phenomena, including life, that ours does.

So we probably shouldn’t wish for any level of weirdness other than our own – but it would still be nice to know why things are as they are. Finding out how would probably mean deriving quantum theory from underlying principles like the constant speed of light which is the foundation of Einstein’s relativity (see “What if... the speed of light were infinite”).

“Only a universe with the exactly right level of weirdness produces life”

page 29). But the sheer universality of quantum theory makes this a far-off prospect, says Brukner. “I’m not even sure that this goal can be achieved.”

According to quantum physicist Sandu Popescu of the University of Bristol, UK, we may have to accept that such questions are not physical, but philosophical. “We can predict exactly what will happen, but to say why it happens, we don’t have a clue,” he says. “It happens because nature is quantum mechanical – that is probably the best answer you will ever get.”



FABRICE COFFRINI/AFP/GTY IMAGES

3. WHAT IF...

TIME WENT BOTH WAYS?

If there's one thing that eats up time, it's working out what time is. It pops up in physical laws all over the place – but never quite as we expect it. In quantum theory, a "master clock" ticks away somewhere in the universe, measuring out all processes. But in Einstein's relativity, time is distorted by motion and gravity, so clocks don't necessarily agree on how it is passing – meaning any master clock must, somewhat implausibly, be outside the universe.

Even odder, neither theory seems to place any restriction on time going backwards. The familiar one-way flow of time is expressed in only one area of physics: thermodynamics. If time flowed both ways, sometimes your coffee would warm up while sitting forgotten on your desk. Dropped eggs might spontaneously reassemble and leap from the floor into your hand. The dead might return to life and live backwards to birth, Benjamin Button style.

The culprit is entropy, essentially the thermodynamic measure of a system's disorder. When the universe was born, matter was randomly distributed throughout its tiny dimensions and it was the same temperature everywhere. Then gravity kicked in, pulling together matter and heated it up to form galaxies, stars, planets and other ordered imperfections. Thermodynamics has been trying to re-establish disorder, increasing entropy every which way it can.

At a local level, entropy increase seems to be associated with information loss. Broken eggs do not reassemble because information about the former ordering is lost to us in the smash. You don't have all the information needed to put Humpty Dumpty together again – and that amounts to a barrier to travelling back in time.

Or does it? "When the story is told like this it appears compelling, but the moment you start looking into more detail, it becomes more convoluted," says Sandu Popescu of the University of Bristol, UK. In classical physics, you could in principle reverse a thermodynamic process if you preserved the information by measuring the trajectories and velocities of all the components of a breaking egg – suggesting that we could reverse time.

So why can't we? One possibility, Popescu thinks, is an information gap intrinsic to the way the quantum world works. Here we are back with the phenomenon of entanglement (see "What if... quantum weirdness were weirder?", left). When a cup of coffee cools, Popescu thinks, continual interactions between molecules of air and coffee



"No theory of nature appears to place any restriction on time going backwards"

4. WHAT IF...

THERE WERE MORE THAN THREE DIMENSIONS?

increase their quantum entanglement. Although you can know what states an entangled particle pair contains, you can't definitively know which one has which state – leading to a continuous sapping of information from the world.

It's still just an idea, Popescu admits. "Quantum mechanics is consistent with our macroscopic phenomenon being driven by quantum rules, but we cannot prove it," he says. And there is a huge sting in the tail: if he's right, in some sense, time may be capable of flowing backwards after all.

Evolution in reverse

That's because in a classical physics calculation, in theory all you need is a system's initial state and the laws of mechanics to work out what will happen for the rest of time. But in quantum mechanics, where a system's evolution is probabilistic, you can specify conditions for the initial state and final states of the system, and both of these conditions will influence the evolution. Apply this idea to the universe as a whole and "information could be coming from plus infinity and propagating back through time", says Popescu.

There's no evidence of any of this so far, Popescu cheerfully admits. "No one yet has investigated it seriously," he says. "It is speculative." But if in the future physics shows that time really can travel backwards, well – in some sense we must already know.

Yes, OK, four dimensions – time is a dimension too, albeit an oddly unidirectional one (see "What if... time went both ways", left). But we've long thought there might be more large-scale spatial dimensions than the up-down, left-right, in-out we are all used to.

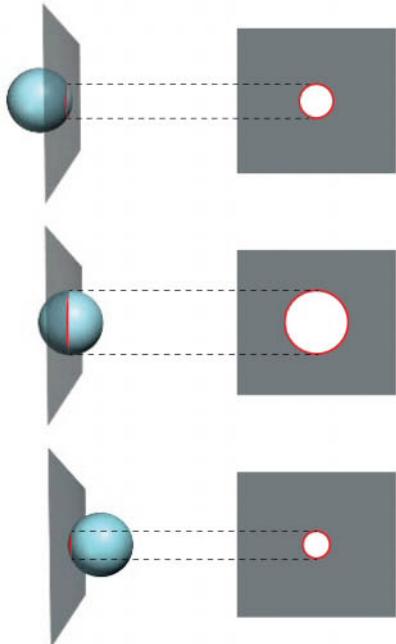
In the late 19th century, British mathematician Charles Howard Hinton suggested that what we perceive as different objects moving in relation to one another could be thought of as single, solid objects in a four-dimensional space passing through our three-dimensional universe. To get a sense of what that means, imagine what a spherical ball looks like observed as it passes through a two dimensional sheet – as a circle whose radius expands and then contracts in time (see "View from Flatland", overleaf).

Adding extra dimensions to the universe is easy enough, on paper at least: you just need additional terms in your coordinate system. The question becomes how we perceive them. Einstein slipped in an additional space-like dimension to his equations of general relativity to explain how mass warps space-time. We don't perceive this dimension directly, but experience it as an acceleration and explain it as the force of gravity.

Some physicists are adamant that more physical dimensions must exist beyond those we can see. In string theory – still most physicists' chosen route to a unifying theory that combines gravity and the forces of the quantum world – the number of spatial

View from flatland

A 3D sphere looks like a circle of changing radius as it passes through a 2D sheet. Similarly, a higher-dimensional object wouldn't be perceived as it really is if it passed through our 3D world



dimensions is at least 10. This gives physicists enough wiggle room to try to explain all of the forces of nature together – but doesn't explain where these extra dimensions are.

Extra dimensions have some odd consequences, too – implying, for example, a multiverse of distinct universes next to one another. Not everyone likes that. "I'm not a fan of the multiverse picture," says physicist Erik Verlinde of the University of Amsterdam in the Netherlands. "Universes that we cannot communicate with are not that interesting to talk about. I think that we should be happy if we can explain the universe that we live in."

Verlinde has been developing a quantum description of space and gravity to replace Einstein's smooth space-time "continuum". In his picture, minuscule building blocks made of quantum information become increasingly quantum entangled and create the seemingly continuous three dimensions of space.

But why three? That question remains open. "A lot of these ideas can be implemented in two, three, four or higher dimensions, so I don't have an immediate reason why there should be three dimensions," Verlinde says. And until someone can find one, tales of dimensions beyond those we can see might not be so wacky after all.

5. WHAT IF...

ANTIMATTER WORLDS EXIST?

Antimatter has always been full of surprises. The first was that it existed. The second was that it didn't.

First things first. In the 1920s, British physicist Paul Dirac managed to marry quantum theory with Einstein's special relativity to explain how tiny, fast-moving fundamental particles such as electrons work. But his austere beautiful unifying equation, honoured with a plaque in London's Westminster Abbey, had an unwanted consequence. For every matter particle like an electron, it predicted the existence of a second particle that was the same, but opposite in things like electric charge.

Dirac initially brushed this under the carpet – out of "pure cowardice" he later said – but three years on, the antimatter version of the electron, the positron, was discovered in cosmic rays. Since then, as the standard model of particle physics was built on the foundation that Dirac and others laid, a very different problem has emerged. Antimatter shouldn't just exist, it should be abundant: every time a matter particle is made, an antimatter particle should also be conjured from the void. "We should have a universe half full of antimatter," says Michael Capell, an astroparticle physicist at the Massachusetts Institute of Technology. So where are these particles?

They can't be near us because matter and antimatter mutually "annihilate" whenever they meet, and we would notice the flash of

X-ray energy produced when they do. Various small-scale particle behaviours might allow there to be slightly more matter than antimatter, but none of these effects is nearly big enough to explain the size of the discrepancy we see.

Perhaps, then, the missing antimatter is elsewhere – in stars and galaxies made exclusively of the stuff, much as our sun and Milky Way are made solely of matter. Stars made of antimatter would give out the same light as ordinary stars, but also a wind of antiparticles, just as our sun gives out matter particles. When these antiparticles come into contact with ordinary matter outside their galaxy, they should produce X-rays that would again be visible across the universe.

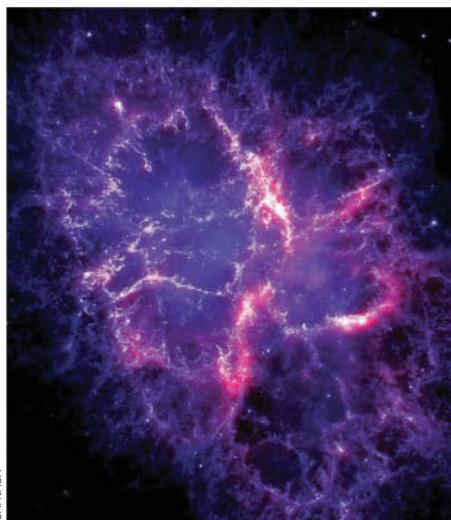
One in a billion

We are yet to see anything of that ilk either, but the Alpha Magnetic Spectrometer (AMS) is performing a more direct test. This giant particle detector, lofted onto the International Space Station in 2011, can sort matter from antimatter in passing cosmic rays.

Positrons and antiprotons can be made relatively easily in today's universe, for example when high-energy particles collide in the strong magnetic fields around dead stars. The real prize would be something bigger. Most helium was made in the first few minutes of the universe's existence, so to find anti-helium could mean that the same process created the expected large quantity of antimatter. Stars are the only places where carbon and heavier nuclei can be made, so a single anti-carbon nucleus would confirm that there is an antimatter star somewhere in our universe.

It's like looking for a needle in a haystack – you would expect one complex antiparticle for every billion or so matter particles AMS detects, says Capell, who works on the project. The experiment has just about collected enough events to start saying something meaningful, but it is a race against time. The hunt has to be conducted in space, because antiparticles annihilate on contact with our atmosphere, but space is harsh on technology. "AMS has been working like a champ but we can see that it is ageing," says Capell. In 2014, one of its four cooling pumps stopped working – a worrying development for an experiment designed to last until 2024.

So fingers crossed for something soon to overturn the evidence of our eyes – that we live in an entirely matter-dominated universe. ■



ESA/NASA

Stuart Clark is a consultant for *New Scientist*

Flipping the birds

Millions of years ago, strange opposite birds ruled the skies. How did we end up with something so different, asks Jeff Hecht



JUAN CARLOS LEAL and José Bonaparte were lost in a thick, thorny acacia forest in north-west Argentina when Leal stumbled on the bones. The big ones turned out to be from a new long-necked dinosaur species. But the 60 small bones they found alongside were puzzling. They were far too small to be from dinosaurs.

Intrigued, Bonaparte flew to London to show them to a fossil expert at the Natural History Museum. Cyril Walker immediately recognised them as a rare find – the remains of ancient birds. By this point in the 1970s, some palaeontologists suspected that all birds had evolved from flying dinosaurs, but the idea was not yet mainstream.

Looking closely, Walker discovered that the fossil shoulders and feet had grown quite differently to those of modern birds. A key ball-and-socket joint in the shoulder was reversed. This was a whole new avian category, not just a new species. In a short paper published in 1981, he named the fossils *Enantiornis leali*: Leal's opposite bird.

Now we know that *Enantiornis* wasn't an evolutionary oddity. Millions of years ago, the skies were full of such creatures. Then, some 65 million years ago, an asteroid hit Earth and opposite birds were relegated to the history books along with the vast majority of dinosaurs. The only survivors gave rise to every bird alive today.

Therein lies the mystery. How did modern birds escape total annihilation? Despite looking remarkably similar to their opposite cousins, they must have had some mysterious features that allowed them to survive the devastating impact. By looking at the subtle differences between modern birds and their extinct opposite cousins, palaeontologists are trying to piece together what made ➤

The fish-eating opposite bird
Longipteryx rocked a mohawk
and ferocious teeth



PHOTOGRAPHS BY STEPHANIE ABRAMOWICZ FOR BIRDS OF STONE; CHINESE AVIAN FOSSILS FROM THE AGE OF DINOSAURS BY LUIS M. CHIAPPE AND MENG QINGJIN

HATCHING A CHICKENOSAURUS PLOT

Birds lost their teeth between 130 and 70 million years ago (see main copy), but hints of them remain in chickens. A decade ago, geneticists found a mutation called *talpid*² in chicken embryos. It is fatal, but by looking at embryos before they hatched, the team figured out that it caused them to grow tiny little tooth buds. The finding helped inspire palaeontologist Jack Horner - a technical advisor on *Jurassic Park* - to propose

a project that would genetically engineer a "chickenosaurus". It isn't as crazy as it seems. Two years ago, Bhart-Anjan Bhullar at Yale University and his colleagues took a step in that direction when they engineered a chicken embryo with a snout - a bit like a dinosaur. The work involved comparing gene activity in chicken and crocodile embryos. The two animals share a distant common ancestor with dinosaurs. The geneticists then

tweaked the chicken genes to be more crocodilian.

We're still a long way from meeting a chickenosaurus, but don't knock it. Bhullar's work was a huge achievement that helped show evolution in (reverse) action. And it does suggest that genetic studies like these could one day succeed in turning the evolutionary clock back more than 130 million years - to the time when opposite birds and modern birds diverged.

Tweety such a remarkable survivor.

Opposite birds split from modern birds between 150 and 130 million years ago, and for more than 60 million years, both types of flying beasts shared the skies. Opposite birds were just as diverse and numerous as the ancestors of modern birds – at one time, they were even more diverse. Two decades after Leal and his colleagues whacked their way through the Argentinian bush, Chinese farmers led another team of palaeontologists to a bed of fossils in China. It was stuffed full of ancient winged things, the most varied by far were opposite birds. Some 50 to 60 species have now been found on every continent except Antarctica.

When birds had teeth

The most noticeable differences between the two groups were their sizes and habitats. Opposite birds were much smaller, with adults ranging from the size of small songbirds to that of vultures. They lived in forests, unlike the ancestors of modern birds, which hung about near shorelines. So far, however, it is not clear that these differences would have doomed opposite birds to extinction.

Other differences were subtle. Yet the group's complete demise could not have been random, says Gareth Dyke of the University of Debrecen in Hungary. They must not have been doing something the survivors were doing, otherwise we would still have opposite birds – or rather their descendants – flitting around our forests today.

The differences in their bones, the very feature that led Walker to define *Enantiornis* as a whole new class of bird, would not have been visible when covered in muscles and feathers. There is also no evidence that they would have affected flight, says Dyke. Recent studies show that both groups had strong flight muscles and small feathered thumb-like flaps called alulae to precisely control their trajectory. Dyke says this suggests the two types of birds flew in very similar ways.

The wings of some opposite birds did have one unusual feature – little claws peeping out from under the feathers – but it is likely that at least some ancestors of modern birds had these as well. Today, they are still seen on the juveniles of the ground-dwelling hoatzin, a large, tufted rust-coloured bird that lives in South America. The claws help young birds to climb trees.

What of their diets? Both types of birds evolved from toothed dinosaurs and for a time, both groups kept their teeth. Some of

Many opposite birds had impressive tail feathers



the older opposite bird fossils from China have impressive choppers (see picture, above left). But then so did the ancestors of some modern birds, such as the fish-eating *Yanornis*. By the time of the asteroid impact, many species in both groups had evolved toothless beaks.

Why? A beak is only an advantage if you are a herbivore, says Jingmai O'Connor at the Institute of Vertebrate Paleontology and Paleoanthropology in Beijing. Carnivores just rip and gulp prey for a big hit of energy, and teeth do that well. But plant-eaters need to grind through their food's tough fibres. Some, like horses, have banks of heavy grinding teeth for this, but early flyers would never have got off the ground with these. Instead, they evolved gizzards and light beaks.

Derek Larson at the University of Toronto and his colleagues wondered why the asteroid killed toothed birds that were closely related to modern birds and small toothed dinosaurs, but not beaked birds. On the basis of the diets of living birds, they say it is likely that their ancestors had beaks and gizzards and ate seeds. That could have been an advantage after an asteroid impact. Hard shells would have protected the seeds' nutritious cargo, turning

them into durable reserves that hungry animals could tap for decades, while ecosystems recovered. It is a nice theory, but one that's impossible to test without direct evidence of what the different birds ate.

The hollow bones of both groups offer another clue. They contain air sacs that boost lung capacity, and the sacs of the ancestors of modern birds were larger. Breathing would have been hard as wildfires swept the planet after the impact, so it's possible that modern birds had an advantage there.

EGGY TURN

Ever noticed those little springy white cords attached to egg yolks? Have a look next time you crack an egg. They're the chalazae and they hold the yolk suspended mid-egg, so that it floats in an incubation bath with a constant temperature. They also ensure the developing chick is not damaged when its mother turns the egg. Egg-turning only evolved in modern birds. Opposite birds buried their eggs, so it is possible their eggs didn't have those stringy bits.

Or perhaps all it took was a bit of parental love. In 2004, Zhonghe Zhou and Fucheng Zhang, also at the Institute of Vertebrate Paleontology and Paleoanthropology in Beijing, revealed that they had discovered the fossilised embryo of an opposite bird, still curled up inside its eggshell. The remarkably well-preserved fossil has an almost fully developed skeleton, wings and even tail feathers. In July last year, partial wings belonging to two very young opposite birds were discovered preserved in a 99 million year old piece of amber.

"Perhaps all it took for modern birds to survive was a bit of parental love"

Together, these finds suggest that newly hatched opposite birds were much more mature than modern chicks. They came out of the egg fully feathered, ready to run and perhaps to fly. As a result, it is unlikely they got much parental care. Parents probably brooded their eggs, but once the chicks hatched, they fended for themselves.

Where the eggs hatched is also odd. We know that adult opposite birds mostly lived in forests and had feet made for perching on branches, but fossil nests show they began their lives in eggs partly buried in soil. The ground-dwelling bush turkeys, or megapodes, of Australia are a modern example of this. Their chicks dig their way out of the ground after hatching, a bit like turtles. Megapodes are also the only living birds with superprecocial young, says David Varricchio of Montana State University. "[They] are completely independent of their parents. They hatch and run off on their own."

That may have made life particularly challenging on post-impact Earth. Gerald Mayr of the Senckenberg Research Institute in Frankfurt, Germany, says unprotected young would have been more vulnerable to predation. Given that many species of dinosaurs that were wiped out after the asteroid also had superprecocial young, could a bit of parental care have made all the difference for the ancestors of modern birds?

At the end of the day, each of these factors may have been only a minor benefit for Tweety's ancestors, says O'Connor. But when it comes to survival, every little bit helps. ■

Jeff Hecht is a freelance writer based in Boston, US

We're moving closer to understanding how anaesthesia works, finds Philip Ball

WHEN THE LIGHTS GO OUT

COUNT slowly backwards from 10. Before you reach seven, you'll be out like a light. Without anaesthesia, surgery would be, and once was, excruciating. Yet, as anyone who has been put under will attest, general anaesthesia is a pretty drastic medical intervention itself: a sudden and total shutdown of consciousness. It's not hard to see it as a little foretaste of death. General anaesthesia was first used for surgery in the 1840s. The shocking thing is that we still don't really know how it works.

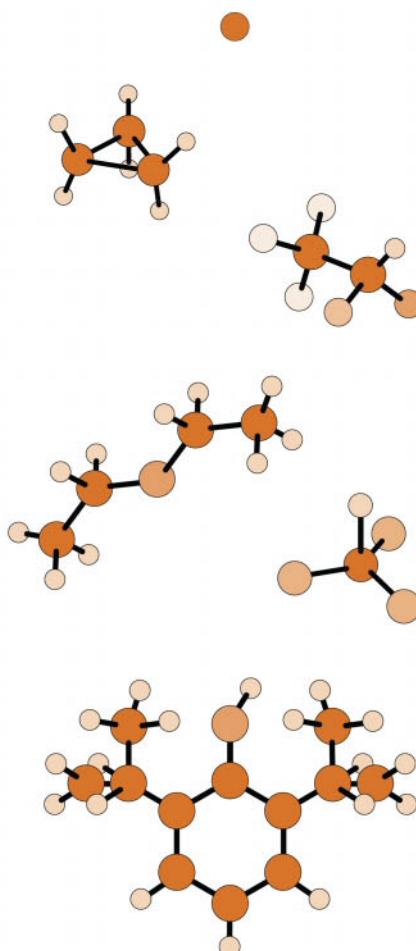
We do know that anaesthetic agents suppress signalling between neurons in the brain. We think we know which molecules the agents hit. But just how they do their silencing job is a mystery.

Fortunately, this lack of knowledge doesn't stop anaesthetists wielding the drugs effectively. However, a clearer picture of what happens could not only help to avoid the rare but very real dangers of anaesthesia, but also help us develop more precisely targeted drugs and give us a better idea of consciousness itself, and what it means to toggle it on and off.

Recently, we have uncovered a few more clues as to how it all works, through research in biochemistry and more surprisingly in biophysics. But just how close are we to solving the mystery of how anaesthesia turns out the lights?

Many drugs work more or less in a "lock-and-key" fashion. They block biochemical processes because they precisely match the shape of specific molecules' binding sites. And this seems to be how some classes of anaesthetics, including barbiturates, interrupt communication between our neurons.

But there is a befuddling diversity to the substances that can knock us out: from large-molecule steroids to untethered individual atoms (see diagram, right). Consider xenon, a gas that exists as lone atoms that don't undergo ordinary chemical interactions with anything else. These bland, unresponsive balls are about as far away as you can imagine from the exquisitely shaped molecules of most



From the top: xenon, cyclopropane, halothane, diethyl ether, chloroform, propofol

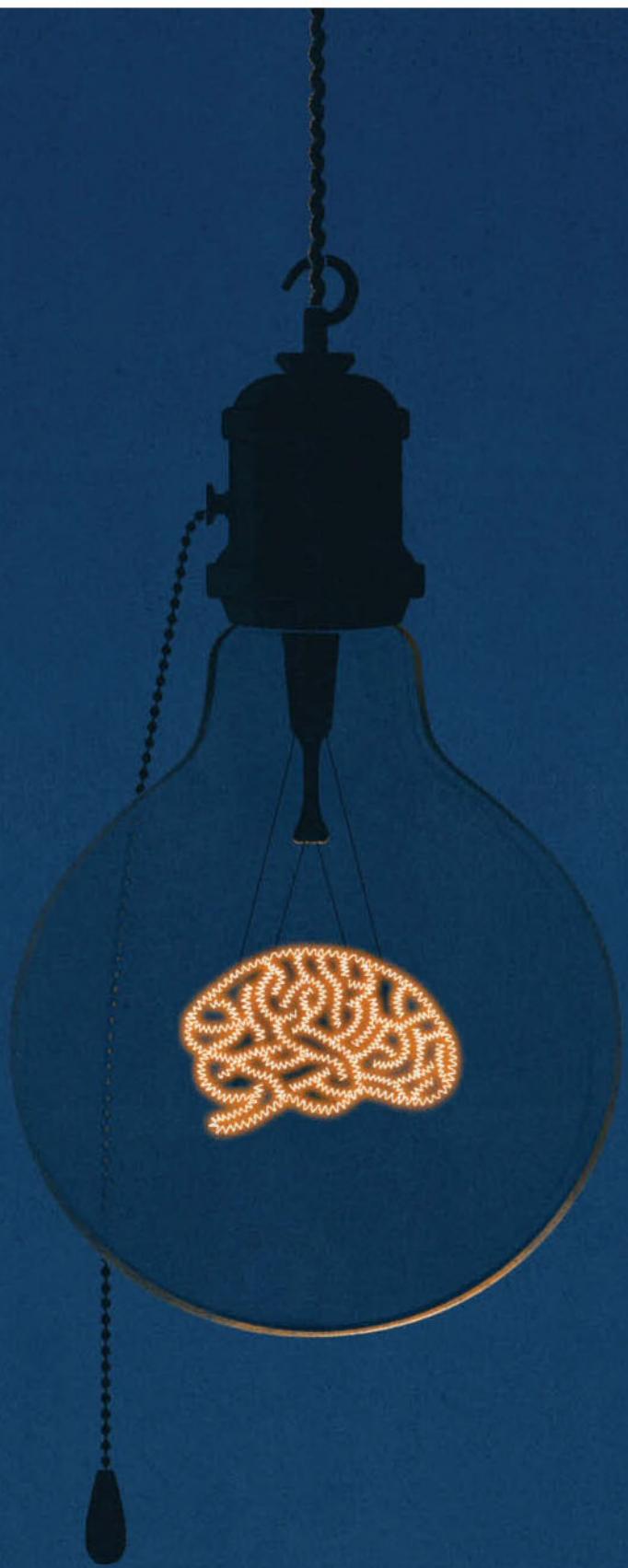
drugs. Yet today xenon is a fairly common anaesthetic. How can such a simple substance have such a remarkable effect?

Xenon isn't very compatible with water, which prefers charged particles such as salt ions. Because it doesn't have concentrations of positive or negative charge, xenon sits more easily in a nonpolar environment, like the fatty insides of the membranes around our cells.

This, it turns out, is a common feature of many anaesthetics, from nitrous oxide to chloroform, as German pharmacologist Hans Meyer and British physiologist Charles Overton discovered more than a century ago. The pair independently found that the potency of many anaesthetics corresponds with how readily they dissolve in olive oil: the more soluble the substance, the less of it you need to induce unconsciousness. This relationship is even stronger when it comes to their solubility in real membranes like those of cells, made from fatty acids called lipids. Meyer and Overton both figured that anaesthetic agents must accumulate within the membranes and make them swell or distort, altering their ability to transmit signals.

Electrical signals pass along nerve cells through the movement of positively or negatively charged ions. These flow in and out of the cell via ion channels – proteins in the cell membrane that are arranged into the shape of a tunnel. When the difference in voltage between the inside and outside of the cell reaches a critical threshold, this triggers a signal and neurotransmitters are released at the synapse, or junction, with neighbouring cells. These chemicals flow across the gap and latch onto ion channels at the next cell, where, depending on the type of neurotransmitter, they either boost or dampen onward signalling.

The Meyer-Overton model suggested that anaesthetic molecules might be absorbed into cell membranes at the synapses and block cell-to-cell signalling, possibly by causing the sheets of fatty molecules to



"There is a befuddling diversity to the substances that can knock us out"

swell and shut the ion channels.

It was a neat idea, but too simple. In 1997, chemist Robert Cantor of Dartmouth College in New Hampshire suggested a more sophisticated process. He argued that rather than indiscriminately swelling the membrane, anaesthetics jostle the molecules around ion channels, affecting how they are packed together and changing the curvature of the membrane itself. But details of how this might work remained sketchy, and the resulting changes would be so small that it was hard to

see how they could make much difference.

But now there are hints that such small effects can indeed have big consequences. Physicist Ben Machta at Princeton University and biophysicist Sarah Veatch at the University of Michigan in Ann Arbor think that anaesthetics may affect the "critical temperature" of the cell membrane, making the system sensitive to slight changes.

General anaesthesia has been used during surgeries for almost two centuries

This is a basic concept in physics: at a critical point or critical temperature, a system can undergo an abrupt change of its state. A magnet can lose its magnetism, or a mixture of two liquids can separate, for example.

In 2012, Machta and Veatch, working with physicist James Sethna at Cornell University in Ithaca, New York, argued that close to a critical temperature, the molecules that make up the cell membrane are constantly rearranging themselves. In the membrane there are "rafts" of regularly packed molecules, mostly cholesterol and saturated fats, that drift within a more disorderly matrix of unsaturated fats.

The researchers assumed that some ion channels only open, or open most easily, when surrounded by particular molecules – a cluster of cholesterol, for instance. Close to the critical point, these molecules are more active, so the rafts are constantly appearing and dissolving all through the membrane. In this case, there is a good chance the ion channel will acquire the surroundings it needs to open.

Tipping point

If, however, anaesthetic molecules join the membrane and alter the temperature needed to reach this critical state, the ion channels won't get exposed to the same variety of environments and may stay shut. "Cells, or drugs, could fine-tune the activity of channels by changing the membrane," says Veatch. "Maybe this is what happens in general anaesthesia."

In a series of experiments, Machta and Veatch showed that alcohols with anaesthetic properties, such as ethanol, do indeed lower this critical temperature, meaning the membrane would have to be colder than usual for the rafts to acquire such dynamic variation in shape and form. What's more, they also found that two lipid-loving drugs that ought to act as anaesthetics according to the Meyer-Overton rule but don't, fail to alter this critical temperature.

In contrast, some compounds, such as hexadecanol, raise the critical temperature. So would they suppress anaesthesia? Last year, that's just what Machta and Veatch found. In tadpoles at least, hexadecanol can counteract the anaesthetic effect of ethanol.

Machta says they are hoping to test their ideas further by finding ways of looking directly at the environment surrounding ion channels at the molecular scale.

A more exotic possibility is proposed by biophysicist Luca Turin of the Alexander Fleming Biomedical Sciences Research Centre



PUTTING YOU UNDER

Routinely used for surgery since the 1950s, general anaesthesia is now very safe, even if the details of how it works aren't fully understood (see main story). The risk of death from anaesthesia is estimated at around 1 in 100,000. The most common complications are mild: nausea, sore throat, headache and temporary confusion (see "When anaesthesia goes wrong", right).

There's a degree of trial and error in finding the right dose for each patient, says anaesthesiologist Nikolaus Gravenstein of the University of Florida College of Medicine. "We look to see if that response is about what we expect, or more or less, and adapt accordingly." You can track the effect of anaesthetic

using a technique called bispectral index monitoring, which measures several brain parameters, but this is expensive and only used in high-risk cases.

There's always the chance of equipment failures or human error, such as forgetting to refill a medication that has run out, says Gravenstein. But genetics can also influence our response to anaesthetics. People with Down's syndrome can be particularly at risk of complications. And there are many rare genetic diseases that increase the risk of problems such as airway blockages and heart, liver or kidney disorders.

Variants in the 60 or so genes that make the enzymes responsible for breaking down certain drugs can also cause

problems, says Merlin Butler at Kansas University Medical Center. "If a person is an ultra-rapid metaboliser or poor metaboliser of drugs such as anaesthetics, they can become toxic leading to serious side effects," he says. Because they are so rare, such genetic conditions are not yet routinely screened for before anaesthesia, but this may change as personalised genetic profiling becomes a regular aspect of medicine.

Most major complications aren't related to the fact that we don't understand the molecular mechanisms of anaesthesia, says Gravenstein. "Although clearly, as we understand them better, we can design better medications to target them."

When anaesthesia goes wrong

Anaesthesia for surgery is routine and safe – but in very few cases, problems can arise

NERVE DAMAGE

About 1 in 5000 people get permanent damage of some peripheral nerves, often in the hands or feet, while under anaesthetic. And 1 in 2000 patients will have temporary nerve damage. This can happen either if a nerve is injured during the operation itself, or because it is stretched or squashed when the person is lying down in an awkward position for a long time. If you were awake, this would make you uncomfortable and you would move, alleviating the pressure. When you're under, that's not an option.

DELIRIUM

After an operation, some people emerge from the anaesthetic into a bewildered state of delirium. This is especially common among older patients or people taking medicines such as antidepressants, but usually resolves within a day or two. In many cases, it may be preventable. Some research suggests that using a lighter level of anaesthesia can reduce the risk of delirium afterwards.

in Vari, Greece. Turin is no stranger to big, if controversial, ideas. He has previously made the case that our sense of smell works by quantum physics. Instead of picking up scent from the shape of particular molecules, he argued that we pick up on their vibrations, which influence electrons jumping across gaps in our olfactory receptors.

Now he thinks some general anaesthetics do something similar. Xenon “has no chemistry and no shape, but it has physics”, Turin says. He suggests xenon might insert itself directly into proteins and influence signalling. It could do this by providing new, energetically favourable pathways along which individual electrons would use the magic of quantum physics to jump from one part of the molecule to another. If an anaesthetic did use such electron currents, this should show up as changes in a property called spin, which is

WAKING MID-OPERATION

Perhaps one of the most worrisome problems is accidental awareness – partially waking up mid-operation because you are not getting enough anaesthetic. That might not be as bad as it sounds, though: most patients who experience it feel no pain, but may remember being in theatre. Often the waking episodes happen before or after an operation.

Still, it can be very alarming. As a child, Fredrik Lloyd, a poet now living in Oslo, had several operations on his foot and stomach at Great Ormond Street Children’s Hospital in London. One of them he never forgot. “I woke quite suddenly and sat up during an operation. I was wide awake, and someone was cutting into me,” he says.

“I remember the green walls, which had all sorts of instruments hanging on them. I remember large saws, drills, pliers and so on. The person cutting me up started telling someone on the other side of the table off, shouting at them... I must have fallen unconscious again. I wasn’t aware of any pain.”

It’s estimated that one or two out of every thousand patients experience a degree of awareness

under general anaesthesia. Some, unlike Lloyd, find they are paralysed and can’t signal their condition. Fortunately this rarely lasts more than a few minutes, but some people who wake during surgery later develop post-traumatic stress.

DEATH

The vast majority of deaths that occur under general anaesthesia aren’t caused by the anaesthetic itself, but it does happen. In very rare cases – one out of every 20,000 patients – people can have severe allergic reactions to the drugs. For five per cent of these people it can prove fatal, although most make a full recovery.

More often, people die because of complications related to the condition the surgery is intended to treat. It is very rarely due to errors made by the medical staff that aren’t recognised in time. Perhaps the most famous case in recent years was that of the American comedian Joan Rivers, who died during an operation on her throat. An examination of that case suggests it was probably human error, and not an adverse reaction to anaesthesia, that proved deadly.

detectable for lone hopping electrons but not when they are paired up in chemical bonds. And in fruit flies knocked out by drugs including xenon, nitrous oxide and chloroform, Turin and his team have indeed detected increases in electron spin.

It’s hard to know what to make of such broad-brush measurements. But Turin’s challenge to conventional wisdom doesn’t stop there. He points to some experimental evidence that anaesthetics don’t target synaptic membranes at all, but instead bind to membrane proteins in mitochondria, the compartments within cells that produce energy. “What is the connection between mitochondria and neuronal function?” Turin says. “Nobody knows, but there the treasure is buried.”

The mainstream view, though, sticks with synaptic ion channels – and largely with the

notion that anaesthetic molecules hit them directly, not via some influence on their membrane environment. Some of the most potent, intravenously delivered anaesthetics do seem to bind directly to such ion channels. And the activity of these drugs is highly sensitive to shape – mirror-image forms of the same molecules have different potencies – which points to a conventional lock-and-key mechanism.

Ethereal ideas

Stuart Forman, an anaesthesiologist at Massachusetts General Hospital in Boston, says there is some evidence that even inhaled, small-molecule anaesthetic agents bind directly to ion channels. Besides, says neuroscientist Peter Århem of the Karolinska Institute in Stockholm, Sweden, the fact that anaesthetic molecules prefer fatty environments doesn’t necessarily mean that they head for the membranes as some of the other theories suggest. They might instead stick to water-repellent cavities on the proteins in the ion channels. “But I would happily welcome better explanations,” he says.

So, however intriguing these new physics-based ideas may be, they have their work cut out if they are to persuade many experts. Forman has learned to be wary of theories based on biophysics rather than biochemistry. “I call them zombie theories,” he says. “Experiments can’t breathe any life into them, but neither can they be definitively killed off.”

Zombie theories or not, solving the mystery of anaesthesia is more than an academic matter. Sometimes there are serious complications (see “When anaesthesia goes wrong”, left). Death from anaesthesia is rare, but it does happen; less serious side effects are fairly common. Knowing what is really going on should let us design better drugs. Here Forman thinks that the more potent lock-and-key molecules are the most promising, because they are more amenable to design – you can’t, after all, do much to tune the effects of an agent like xenon. What’s more, these more powerful drugs can be used in lower doses, and can hit their targets more selectively.

The case isn’t yet cracked, but the latest theories could provide opportunities to limit potential harms. At the very least, they show how inventive we are forced to be in trying to understand what really goes on when the lights go out. ■

Philip Ball is a writer based in London

Inside the venom factory

Nick Casewell extracts venom from the world's most lethal snakes. And he is developing an antivenom that will be nothing short of revolutionary

WE HAVE a hospital just across the road, with a store of our antivenoms," says biologist Nick Casewell. That's good to know, given that we are in a room stacked floor to ceiling with boxes holding the world's deadliest snakes. There are rattlesnakes, puff adders, black mambas and more – if it can kill a human, it's here. With about 250 animals from 40 different species, it's one of the largest collections of venomous snakes in Europe. And it's milking time.

Casewell and his colleague Paul Rowley are about to collect the venom of four vipers from equatorial Africa. We are in the Alistair Reid Venom Research Unit, which sends supplies of venom around the world to make antivenom. But Casewell is also working on a project that could save tens of thousands more lives each year.

Looking around, every snake's box lists its species and the antivenom required if you are bitten. And therein lies the problem. An antivenom only works for a handful of species at most. If you get bitten, you need to know what kind of snake it was and hope that someone nearby has exactly the right concoction to give you. If not, you're in trouble. Surveys estimate that around 125,000 people die from snakebites every year. The true figure is probably much higher, Casewell says. "Snakebite is a major problem, but the attention it receives is almost nil."

Casewell has seen first-hand the devastation bites can cause, when capturing Senegalese saw-scaled vipers for his unit and when setting up a snakebite project in Kenya. "We visited hospitals with patients who had been bitten by spitting cobras. Some of them had horrific wounds," he says.

Snakes can kill and maim in various

PROFILE

Nick Casewell (far right) is senior lecturer and Wellcome Trust research fellow at the Alistair Reid Venom Research Unit, Liverpool School of Tropical Medicine, UK

gruesome ways, including by paralysing the respiratory system or causing catastrophic tissue death. But more than half of deaths are the result of what Casewell calls "blood disturbances".

That's the speciality of the Gaboon viper, which Rowley is just about to release on to the floor to be milked. Symptoms include intense pain, internal bleeding and an extreme drop in blood pressure. Though its venom is not quite as potent as, say, that of a black mamba, Gaboon vipers have the longest fangs of any snake and the deepest bite, and can inject the greatest amount of venom.

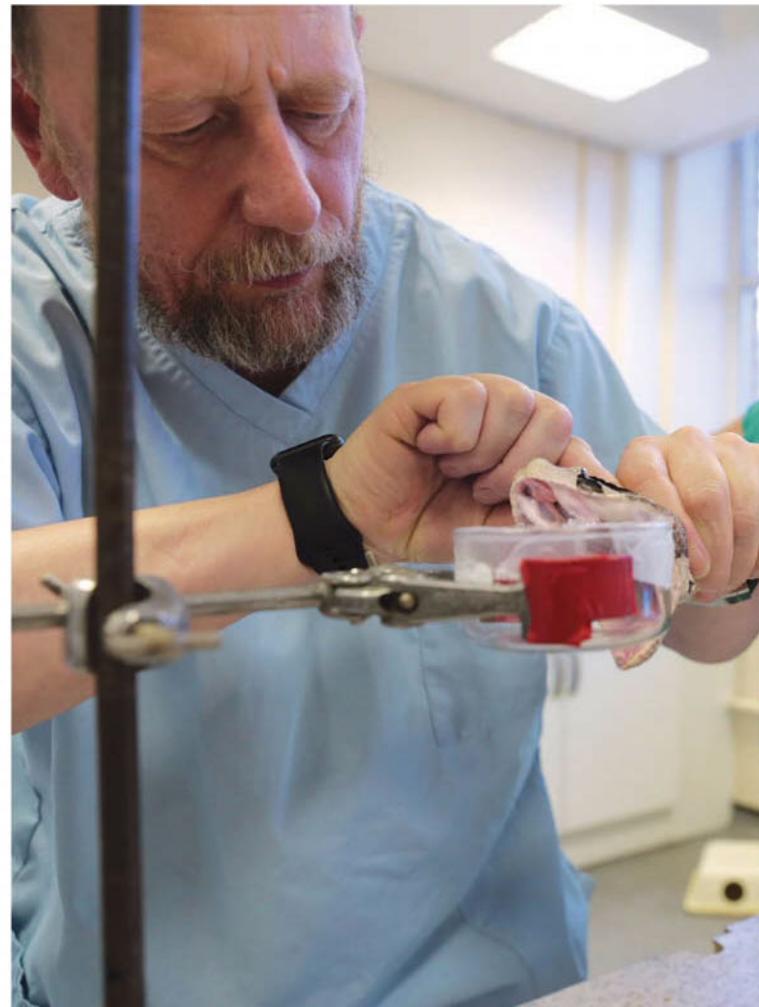
Rowley, who has managed this herpetarium for 24 years, uses a hook to take the snake from its box. He always handles the dangerous end and has been bitten three times. It's a low strike rate, given that he has been milking snakes for all that time. Once the snake is on the floor, Casewell holds it down with a section of plastic pipe attached to a

broom handle. It's the best thing for the job apparently. "I made it in the 90s," says Rowley. The pair are calm despite the situation. The writhing viper escapes several times before they get it under control.

"Fat-bodied vipers in particular are so strong," says Casewell. "There's always a moment when you've got the snake restrained using the tools and you have to switch to using your hands. That's the moment of greatest risk."

But once Rowley has grasped the snake behind its head, the tension eases slightly. The pair carry the animal to a table where a membrane-covered jar awaits. Rowley touches the snake's snout to the glass, and its mouth instinctively springs open. Long fangs swing forward and the snake plunges them through the membrane. Thick yellow venom drips from its fangs and pools inside the jar.

Some of this venom will be used to make antivenom the traditional way. This method





Left: Milking a Gaboon viper is all in a day's work for Nick Casewell and Paul Rowley, who always handles the dangerous end

Above: Rhinoceros viper waiting to be milked

Right: Wrangling in action

Below: Door barriers and a range of tools help prevent snake escapes



has barely changed in over a century: you inject venom in non-fatal doses into a horse or sheep, then extract the antibodies it produces. But it's far from ideal, because the antivenom contains numerous animal proteins that can induce severe allergic reactions in people. "If they weren't life-saving treatments," Casewell says, "they would have a hard time passing medical safety standards."

Casewell and his colleagues are taking a different approach. Though each species' venom is unique, all contain a cocktail of 50 to 200 proteins, and only 20 or so of those are really harmful. The team is working to identify the key toxins that make you bleed to death. Casewell will then immunise mice with them. The resulting antibodies should combat the lethal effects of any venom from half of all snakebites. "If you're bitten and you're bleeding, this one antivenom should save you regardless of the snake," says Casewell.

And the snakes win too. Using a technique

called monoclonal antibody production, he plans to clone the antibody-making cells from the immunised mice to generate a culture that will produce an endless supply of all-round antivenom. That will remove the need to use animals to produce it year after year, and largely solves the allergy problem too. "This type of approach has the potential to completely revolutionise the field of antivenom," says Casewell.

Back at the venom unit, Casewell and Rowley gently return the viper to its box and transfer the venom to a vial that goes in the fridge. They have three more snakes to milk. But having to work so intimately with such lethal animals is a risk worth taking. "When I see first-hand the patients who are suffering, the destitution and poverty that these people live in and the effect that snakebite has on not only them but their families, it's a powerful motivator." ■

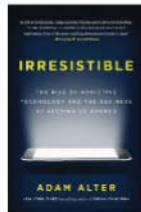


By Sean O'Neill

Turn on, touch in, drop out

Our tech is fine-tuned to keep us hopelessly hooked, finds **Kate Douglas**

Irresistible: Why we can't stop checking, scrolling, clicking and watching by Adam Alter, Bodley Head



MY NAME is Kate and I'm not an alcoholic. Nor am I addicted to cycling. I have been known to enjoy both however –

sometimes simultaneously, and not necessarily in moderation. But as far as I know, I'm not addicted to anything.

If I keep this up, I could soon be in the minority. Apparently, half of the developed world is addicted to something, and the numbers are growing. But where once the bulk of our addictions were to substances, now they are to behaviours – things like online gaming, posting on Facebook and Instagram, binge-viewing on Netflix, and obsessively checking emails and mobile phones. This 21st-century pandemic is the subject of Adam Alter's *Irresistible*, a book which lives up to its title.

We used to distinguish between addicts and others, a view Alter is quick to dispel. We all have the potential to become addicted given the right/wrong environment. It's not you – it's the world you live in that makes behavioural addiction so very likely. In just a few years, he explains, technology and the media have become adept at the lucrative business of gaining and holding our attention. Today's high-tech environment is addictive by design.

You might doubt your iPhone or Fitbit use is an addiction. Until recently, neuroscientists would have agreed. But now we know



Phone-checking: in terms of brain chemistry, not unlike drug-taking

creative destruction of *Tetris* is so compelling, what makes the "juice" in *Candy Crush*, why *World of Warcraft* is so toxic, and how "colour coding" (adding coloured tags to different bits of computer code to see which are used most) has revealed that gamers will spend three times as long on a quest to kill as on one to save. And roll up for the "dollar auction" to find out how so-called predatory games are designed to trap you. There are characters galore, and statistics to make you gasp. It's very entertaining.

Irresistible is not all fun and games, though. Alter is concerned about the growth of behavioural addiction and has plenty to say about how we might keep it in check. That's tricky because going "cold turkey" is not an option; we can't live without technology.

But we can reduce temptation. In a chapter amusingly titled "Never get high on your own supply", Alter notes that the people who design, make and write about addictive technology often strictly limit their kids' use.

We can also use tech to motivate good behaviours. Meet SnuzNLuz, the alarm clock with a hotline to your bank – it donates to your least favourite charity when you press the snooze button. And we have the know-how to create experiences that are compelling but not addictive. Above all, we need to recognise that Instagram, multiplayer games and mobile phones are so enticing because they meet basic human needs.

Luckily for all of us, we also have low-tech ways to fulfil our desires. ■

addictive behaviours produce the same brain responses as drug abuse – the release of dopamine deep inside the brain and its uptake by receptors, resulting in an intense feeling of pleasure.

"It's not you - it's the world you live in that makes behavioural addiction so very likely"

Meanwhile, psychologists are finding out more about the nature of addictive behaviours. For example, experiments where pigeons peck for rewards reveal the power of unpredictable feedback and explain why a near-win is more compelling than a guaranteed reward.

Feedback is one of six

behavioural addiction factors Alter explores. The five others are: goals, which should be just beyond reach; progress, through a sense of incremental mastery; escalation, via progressively more difficult tasks; cliffhangers, to provide tension that demands resolution; and strong social connections. "Despite their diversity, today's behavioural addictions embody at least one of those six ingredients," he writes. And *Irresistible* is chock-full of stories that make his point.

The intriguing tale of an app called Lovematic lays bare the tyranny (and genius) of the "like" button. And there's the story of how Instagram slew its more charismatic forebear, Hipstamatic.

Then we discover why the

Inside the volcano

Forget sensationalism: Earth's most dynamic geology needs no hype, finds **Mary Halton**

Volcanoes, Weston Library, Oxford, UK, to 21 May; *Volcanoes: Encounters through the ages* by David M. Pyle, Bodleian Library Publishing

OURS is a restless planet. While we walk unawares over the remnants of massive eruptions, it is easier than ever to train a camera on Mount Etna's latest effusions. The power of Mount St Helens and Pinatubo lives long in memory, in part because their recent activity is well documented, and in 2010 the whole world watched as Iceland's Eyjafjallajökull grounded European air traffic.

It seems odd, then, to imagine a time when volcanoes were the stuff of legend and religious speculation. It is, however, just this evolution of our relationship with Earth's most dynamic geology that Volcanoes, a new exhibition at the University of Oxford's Bodleian Libraries, sets out to explore.

Confined to just one room in the Weston Library, and taking about an hour to explore, Volcanoes cuts an admirable swathe through the history of our encounters with its namesakes – from a carbonised papyrus scroll discovered in the Roman town of Herculaneum after the eruption of Vesuvius in AD 79 to videos of recent activity around the Pacific Ring of Fire.

While extensive prior knowledge is not required, the exhibition does rather necessitate jumping feet first into certain terminology. Volcanologist David Pyle offers a gentler crash course in the exhibition's accompanying book, *Volcanoes*. However, the

texture and intricacy of original illustrations and diagrams by the likes of Jesuit scholar Athanasius Kircher and explorer Alexander von Humboldt are worth seeing in person, as they have been considerably scaled down for the book so as not to produce a publication that would dwarf the average coffee table.

Some surprising revelations include the longevity of volcano tourism, which kicked into high gear after news of Vesuvius's spectacular 1631 eruption spread rapidly through Europe thanks to the recent proliferation of the printing press. Less than 100 years later, visitors to the Marylebone pleasure gardens in London could

witness the "Forge of Vulcan" – a vivid firework display built around a representation of Mount Etna.

By the 19th century, naturalists and travel writers like Isabella Bird and Constance Gordon-Cumming were spending months in Hawaii,

"The book gives voice to those living near sites of volcanic activity, through interviews and poetry"

hiking up Kilauea to witness the "awful waves of unquenchable fire [which] surge and writhe without ceasing".

Several stunning eruptions during the 1800s had worldwide

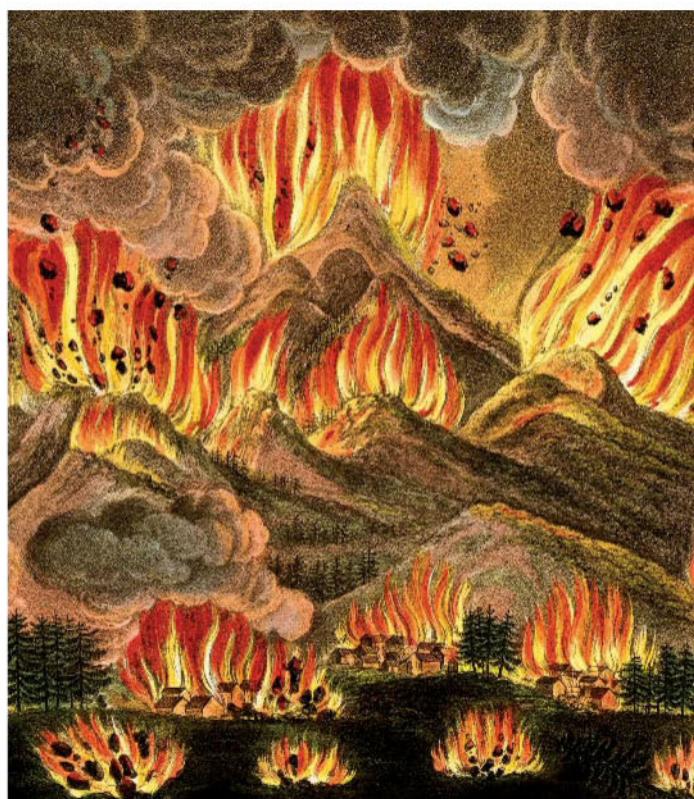
effects, particularly Indonesia's Tambora in 1815. It led to the "year without a summer" of 1816, and caused agricultural devastation across a Europe largely unaware of the eruption. It also yielded the novel *Frankenstein*, when the inclement weather noted by Mary Wollstonecraft Godwin (soon to become better known as Mary Shelley) in her diary kept her holiday party indoors during a trip to Lake Geneva.

In perhaps its most arresting aspect, the exhibition gives voice to those living near sites of activity, with the people of the Caribbean island ofMontserrat recounting their experience of the Soufrière Hills eruption through interviews and poetry. The four-year eruption began in 1995 and devastated the island, eventually burying the abandoned capital Plymouth – once home to 4000 inhabitants – in ash.

Pyle, also the exhibition's curator, weaves his own experiences and insights into the book, as well as drawing on first-hand accounts from throughout history. He also explores what can be done to prepare for the immediate effects and long-term fallout of eruptions.

Despite skewing heavily towards European accounts, because the exhibition draws largely on the Bodleian's own archive, Pyle aims for a global perspective on the human story of the forces that shape our planet. An antidote to the sensationalism of many a supervolcano documentary, Volcanoes is well worth exploring in both its forms. ■

An illustration of the 1783 eruption of Mount Asama in Japan



BODLEIAN LIBRARIES, UNIVERSITY OF OXFORD

Mary Halton is a writer and theatre critic based in London

Unravelling gender myths

We have to take an axe to claims of sex differences, finds **Mel Rumble**

Testosterone Rex: Unmaking the myths of our gendered minds by Cordelia Fine, Icon Books



ONE of the best things about science is its ability to correct itself, spot flaws, poor evidence and bad claims, track the myths they spawn to their roots – and axe them. This process is vital, especially in areas such as race, IQ and gender, where false steps derail fields for years.

Take fruit fly experiments by British biologist Angus Bateman in the 1940s. These ended up underpinning many claims about evolved psychological differences between the sexes. One such was a theory by evolutionary biologist Robert Trivers, which claimed a bigger parental investment by females than males. Claims such as these fuelled myths such as men being more competitive or bigger risk-takers than women.

Psychologist Cordelia Fine questions these myths. In her new book, *Testosterone Rex*, she tackles the biggest myth of all: that every difference can be traced to testosterone. This she labels the Testosterone Rex world view, where differences are touted as “natural” rather than cultural. But if we look harder at the evidence, it doesn’t stack up, says Fine.

Take risk-taking. Girls/women can and do take risks and compete to the same degree as boys/men, says Fine. Seeing sex differences turns out to depend on what you ask women to compete at and which women you ask. So women

are more likely to compete within “more neutral” or “feminine” competitive contexts such as dancing, verbal ability or fashion knowledge. And cultural background and level of economic development seem linked with greater competitiveness; for example, Han Chinese or Armenian girls are as competitive as their male counterparts.

Fine doesn’t deny testosterone’s effects on brains, bodies and behaviour, but it is “neither... king nor... kingmaker”. Testosterone isn’t “the potent, hormonal essence of competitive, risk-taking masculinity” we assume it to be, she says: it is just part of a complex bio-cultural mix.

Fine shows how new studies can upend earlier research by

unearthing those confirmation biases on which many myths of sex differences precariously perch. Back with Bateman’s fruit flies, Fine shows his data “had been biased towards counting the offspring of males”, in part due to less sophisticated methods used in the 1940s, but also because people tend to look for what they want to find without realising it.

“Whether or not you see sex differences in risk taking turns out to depend on what you ask and who”

Aside from research design biases, Fine also notes how social constructions of gender shape the situations people encounter, and their subjective meaning. She

throws out a challenge: “We’re used to thinking of testosterone as... a cause of gender... what if the direction of that familiar pathway also needs to be reversed?”

To answer, Fine lays out some of the more recent research. Take University of Illinois psychologist Dov Cohen and his colleagues, who showed how male testosterone levels can increase in reaction to a small challenge to status. Then there is the behavioural endocrinologist Richard Francis and his colleagues and their work on cichlid fish, which shows how social events regulate the gonads. Or recent findings by Marie-Louise Healy and her colleagues at St James’s Hospital, Dublin, that one in six elite male athletes have testosterone levels below the normal reference range.

Another key tenet of the Testosterone Rex world view is the emphasis on differences between male and female thinking and behaviour. Instead, Fine stresses the similarities. Differences, for her, are idiosyncratic mixes of “masculine” and “feminine” characteristics and gendered qualities. It may be that some differences compensate for others, and end up making the sexes similar, not different.

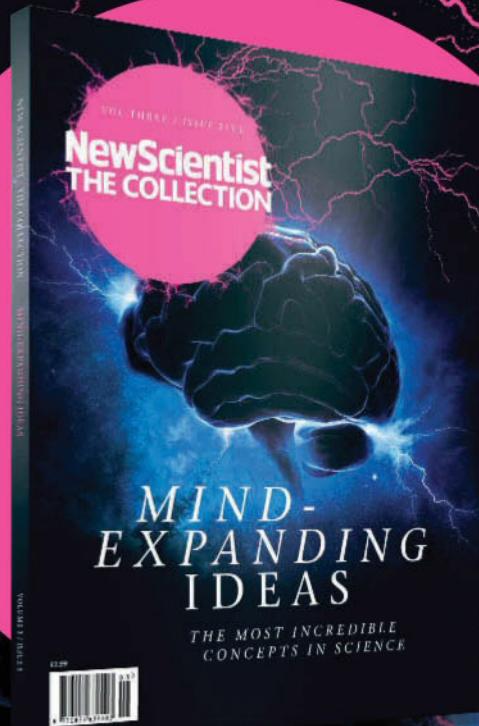
Ultimately, Fine leaves us clear that Testosterone Rex’s old stories are unjustified. What happens next is “a question for our values, not science”, says Fine, arguing for a world where cultural and gender norms sit with evolution, genetics and hormones to take account of all the influences. Then comes the hard work, as she calls on us to imagine the society we want to create. But no fruit flies this time. ■

Testosterone is just one of many factors shaping our identities



LAURENT VAUTIN/PICTURE TANK

Mel Rumble is a writer based in Sydney



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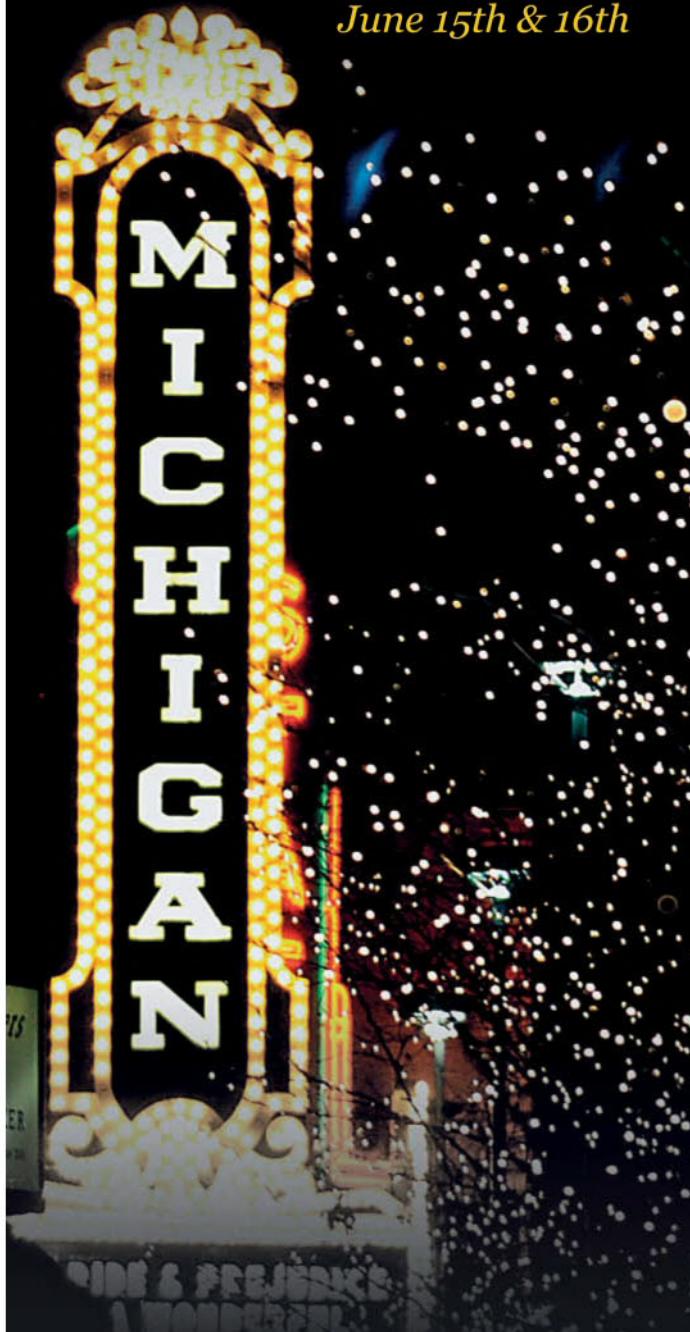
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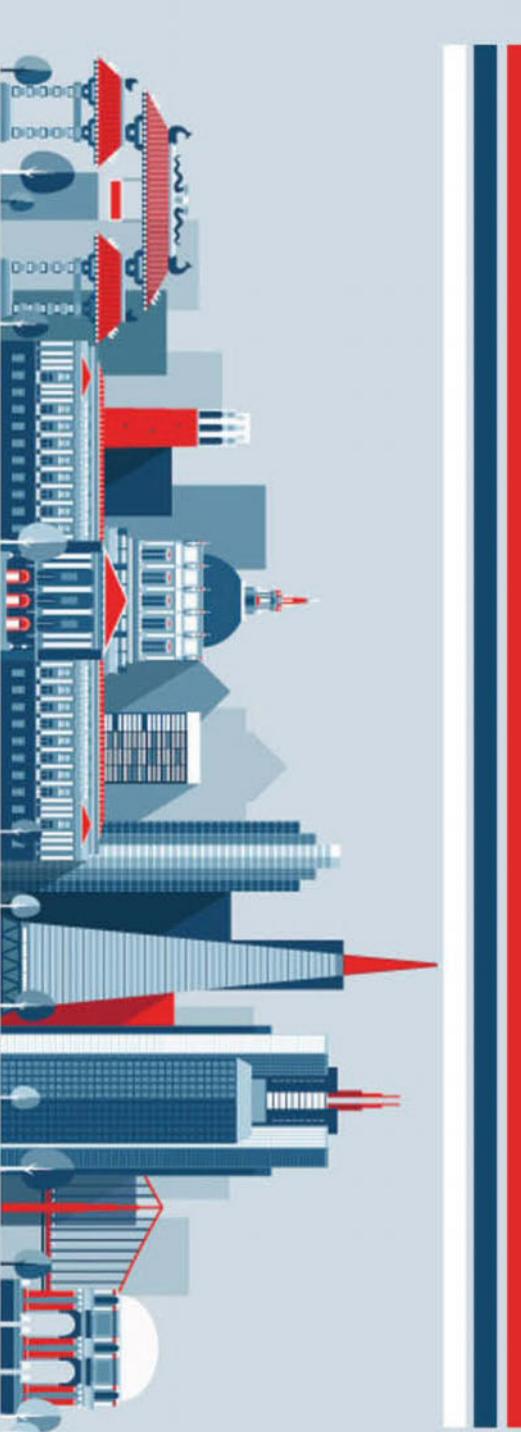
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EDITOR'S PICK**Do we already know this treatment is safe?**

*From Chris Good,
Maidenhead, Berkshire, UK*

Helen Phillips describes the use of propranolol to alleviate the terrifying flashbacks of post-traumatic stress disorder (4 February, p 36). Propranolol was discovered in 1964 and is on the World Health Organization's List of Essential Medicines. It has since been

used to continuously treat millions for high blood pressure. There must be many thousands of people who have avoided PTSD and so been spared terrifying flashbacks by being on it while experiencing or recalling trauma.

A study comparing the incidence of PTSD in those on propranolol with a control population is surely needed.

From Josh Smailes, Lincoln, UK
Phillips describes the use of drugs that inhibit protein synthesis – including propranolol – in treating PTSD. I am concerned that they may not only alleviate traumatic memories, but also cause the loss of other memories that are recalled while the drug is still having its effect.

It is vital that we consider any such possible effects before rolling out the treatment.

Time, gentlepersons, please, time please

From David Werdegar

Naperville, Illinois, US

Anil Ananthaswamy discusses the fundamental make-up of things and the role of time (4 February, p 28). I suggest it would be easier for physicists to resolve the riddle of time if they moved from the abstract to focusing on how we define the passage of time in real life. Independent physicist Julian Barbour's approach to time comes closest to this.

A period of time is nothing more than the ratio of distances covered by reference objects. Measuring a pulse at 72 beats per minute is shorthand for saying that heart muscles contracted by, say, 5 millimetres 72 times while a watch escapement moved, say, 12 millimetres 60 times. The concept is the same if the ratio

involves vibrating caesium atoms.

This model works fine until we approach extremes. At the sub-atomic level, the smallest distance is the Planck length and with nothing smaller to reference against, time as a comparison of changes in distance vanishes.

Similarly, at relativistic speeds the distance a grandfather clock pendulum swings, for instance, foreshortens, so that if it moves 150 millimetres per second when the clock is at rest, it will appear to approach 0 mm per second when it's in a spaceship approaching the speed of light.

From Andy Howe,

Sheffield, UK

You offered quick summaries of current ideas about what time is. These left me with a question.

If, for example, time is caused by increasing entropy or disorder, this raises the same problem as

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"Dreadful. Corals are the canary in the coalmine for this planet"

Kit Drake responds to our report of an unprecedented fourth year of coral bleaching (25 February, p 6)

does the approach in quantum mechanics that "Time... just is" – in which an allegorical clock is required outside of the system in question, even if that system is the entire universe. That is, how would any local collection of particles be affected by remote ones to obey the arrow of time set by the overall system?

Consider knocking snooker balls around a table from a non-random configuration such as a line. Barring a statistical fluke, the resulting pattern of balls would soon appear much more random even though each constituent knock would, according to standard mechanics, be time-reversible. Increasing entropy is an understandable result of individually time-reversible interactions, but I want more explanation of how increasing entropy of the system can cause the direction of time.

*From Martin Baker,
Eskbank, Midlothian, UK*
Ananthaswamy's excellent article reminded me of work by physicist Brian Swingle on the entropy associated with the entanglement of black holes. Swingle has commented that black holes must represent Nature's most efficient quantum computers. This, with the "holographic principle" that a 3-dimensional universe maps on to a surface, raises the distinct and disturbing possibility that we really do live in a computer simulation, running on the event horizon of a black hole.

The meaning of life is what we choose

*From David Archibald
San Diego, California, US*
Teal Burrell discusses the benefits of a sense of purpose and the meaning of life (28 January, p 30).

Arguably the only scientifically demonstrable "purpose" for life is to reproduce itself and sometimes help that new life survive to reproduce in turn.

For humans, the only "purpose" or "meaning" for life is what we choose to bring to it.

For some this is crushing banality, but for others it sets them free. I choose the latter.

Cholesterol correlation can't prove causation

*From Andrew Bamji,
Rye, East Sussex, UK*
Michael Brooks quotes Rory Collins of the Cholesterol Treatment Trialists' Collaboration suggesting that cholesterol deniers are akin to those who believe in a flat Earth (11 February, p 28). Collins argues that "lifestyle factors don't matter, as long as you bring your cholesterol levels

down" and that "statins reduce the risk of coronary heart disease in direct proportion to the reduction in LDL-cholesterol."

Statins bring down cholesterol, and the more you take the more it comes down. Statins also reduce cardiac risk, though not a lot. But that doesn't prove that lower cholesterol reduces cardiac risk. There is evidence statins have an anti-inflammatory action. Lower cholesterol while on statins may merely be a marker that you are taking the statin: inflammation may be the risk for the heart.

The Avandia story is more complicated...

From Jon Arch, Welwyn Garden City, Hertfordshire, UK
Your leader article on access to drug trial data snipes at Avandia, used to treat type 2 diabetes (11 February, p 3). I worked for ➤

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GlaxoSmithKline on drug discovery from 1974 to 2001, where my first boss led the team that discovered rosiglitazone (BRL49653/Avandia), although I wasn't on that team.

It is true that GlaxoSmithKline was fined for withholding clinical data on Avandia. But in 2013 the US Food and Drug administration, unlike the European Medicines Agency, withdrew restrictions on the marketing of Avandia, after a review of all clinical data. You could at least have mentioned that its risks relative to its benefits are a controversial subject.

Hexamethylbenzene dication follows the rules

From Joe McGinnis,
Middlesbrough, Teesside, UK

You report a compound in which a carbon atom bonds to six other atoms (14 January, p 16). Making this hexamethylbenzene dication and determining its structure are interesting and praiseworthy achievements.

But to explain the bonding in this substance doesn't require us to rip up any chemistry textbook.

Just turn back to a preceding chapter, describing how boron forms a family of compounds in which there aren't enough electrons to hold all the atoms together by conventional electron-pair bonds. Instead, the atoms are arranged at the corners of polyhedral clusters, and the electrons are delocalised over the whole structure.

The rules of structure and bonding in boron clusters and related compounds were put forward about 50 years ago by the late Ken Wade of Durham University, UK, and the reported compound obeys them very nicely, as the authors of the paper on it acknowledge.

How hydrogen got into Earth's mantle

From Tim Leeney,
Hartfield, East Sussex, UK

Andy Coghlan says "deep inside the hot mantle, the conditions are right for chemical reactions to turn hydrogen and rock into water" (4 February, p 12). That may well be, but where does the hydrogen come from?

The editor writes:

- We assume it has been there since Earth formed from the solar nebula.

Wood house cooling and the garden bonfire risk

From Roy Harrison,
Verwood, Dorset, UK

The climate benefits of wood-burning stoves are even more dubious than Michael Le Page suggests (4 February, p 22). Many draw the air for combustion from the room in which they are installed. So cold air is drawn into the house, increasing the amount of energy required to heat it.

Sitting in a "cosy" pub next to a very hot radiator while having my feet cut off by the icy gale heading for a roaring log fire intuitively supports this.

If you must buy a wood-burner, get one that draws its combustion air from outside.

From Raymond Gray
Beaminster, Dorset, UK

Le Page refers to a 2010 analysis of particulate pollution that found up to 10 per cent of London's

wintertime air pollution came from wood. A 2014 study, also by environmental scientist Gary Fuller and his team, found little correlation between pollution and daily mean temperature. Instead, wood pollution levels peaked on weekend evenings and school holidays. Fuller interpreted this as resulting from open fires being used as a "decorative or secondary heating source". An equally likely cause is weekend gardeners burning woody waste, and Fuller accepted that such smoke contributes to summertime particulate pollution.

Animal magnetism may work both ways

From Bruce Denness,
Whitwell, Isle of Wight, UK

Henry Nicholls says red foxes apply a magnetic sense to hunting and are more successful when they pounce in a north-easterly direction (17/24/31 December, p 44). Perhaps the prey, distracted by their own magnetic sense, are often facing away from the fox?

That metaphor is out of the League

From John Wallace, Liverpool, UK
I am flummoxed by a rugby ball as an analogy for the shape of Earth (11 February, p 40). I visualise Earth – 21 kilometres longer at the equator than at the poles – more like a hole-less doughnut.

For the record

- Ill effects of statins include 1 in 10 experiencing muscle damage and 1 in 50 diabetes (11 February, p 28).

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TOM GAULD

OBSOLETE SCIENTIFIC THEORIES WHICH WOULD MAKE GOOD HEAVY METAL BAND NAMES



OLD SCIENTIST

What was New Scientist talking about in Marches past?



SCIENTISTS are often derided for having a poor sense of humour. In our 20 March 1958 issue, we hit back with evidence of the “fun” side of science: an extract from the memoirs of physicist Edward da Costa Andrade. He recounted the top-class banter that ensued when a colleague ordered hare soup in Andrade’s college refectory and the dish arrived with a beetle in it. “Waiter, waiter,” he called, “I ordered beetle soup and there’s a hair in it!” A fellow diner took him at his word and advised him to “bring it up before the next refectory committee”, provoking the inevitable quip. Laugh? It’s not reported if they did.

Our wordplay was no less hypodermic-sharp a full 30 years later, when in our 10 March 1988 issue we reported a spat between the news agency Reuters and the *New England Journal of Medicine*. Then, as now, that journal allowed journalists to see its papers before publication, on the understanding that the hacks didn’t let the cat out of the bag early and scoop its big stories. A paper revealing that a daily aspirin substantially reduced the frequency of heart attacks in men was too tempting for Reuters, though, and the agency broke the journal’s embargo. Mutual recrimination and retaliation ensued, inspiring our cartoonist David Austin to draw the cartoon revived above.

By 2007, our Feedback column had been up and running for a number of years and our quotient of humour – or attempts at it – had risen correspondingly. In our 10 March issue, Feedback was picking on product claims, a popular target. Apparently Seabrooke Potato Crisps was proud that its snack had been “cooked in sunflower oil for over 25 years”. Was the same oil used throughout, we wondered.

We’ll let you be the judge of whether scientific humour has improved over the five decades since Edward Andrade told his amusing anecdote. **Mick O’Hare** ■

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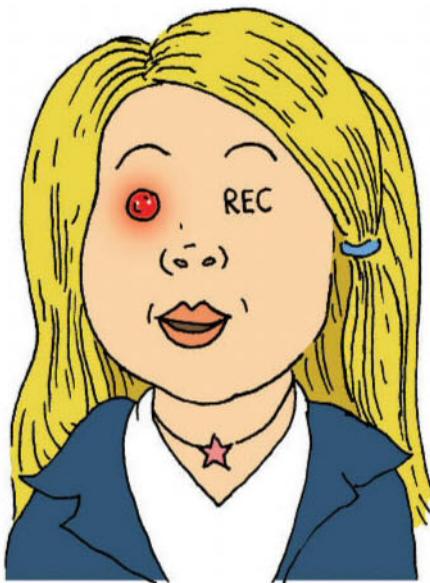
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WHILE many suspect the world is mired in some kind of futuristic dystopia, Feedback finds itself unable to ascertain exactly which writer's fevered imagination we find ourselves stuck in. The latest cause for reassessment comes with the news that German parents have been told to destroy their children's My Friend Cayla dolls over hacking fears.

The internet-connected dolls can listen to queries from children and search for an answer online, but weak security protocols mean the devices could also be hacked to spy on unsuspecting families, or communicate with children.

Importers the Vivid Toy group said it was upgrading the chips to enhance security. Feedback thinks it may also want to update the My Friend Cayla website, which among many selling points boasts: "It's amazing what she knows!".

A SMALL outbreak of fruitloopy was confirmed in the UK recently, following news that Andrew Wakefield had spoken at a

"You know what uranium is right? This thing called nuclear weapons and other things, like lots of things are done with uranium, including some bad things." President Trump offers the White House press corps a science lesson

screening of his documentary *Vaxxed* at Regent's University London, organised by the Centre for Homeopathic Education (CHE).

Readers may recall that the UK was declared free of Wakefield in 2010, after the General Medical Council found him guilty of serious professional misconduct and Wakefield relocated to Texas.

His reappearance on these shores was cause for consternation. Newspapers piled on the epithets: he was "disgraced anti-MMR doctor" in *The Telegraph*, "MMR fraud doctor" to *The Independent*, while *The Times* went with "disgraced MMR fraud doctor" for their front page.

A freshly inoculated Regent's University says it has cut ties with the CHE and would be screening client events more carefully. As ever, prevention is better than cure, thinks Feedback.

THE art world is renowned for two major commodities: great works of art and entertaining rivalries. One

example of the latter erupted after Anish Kapoor, the British sculptor best known for his mirrored pieces such as Chicago's *Cloud Gate* (better known as "The Bean"), secured exclusive rights to use Vantablack, a carbon-nanotube material said to be the world's blackest black.

Cornering the market on a pigment is scarcely new. Legend has it that artist Lucian Freud was so enamoured of the creamy lustre of lead white that he bought the UK's entire remaining stock when it was banned for being toxic. However, Stuart Semple, another British artist, was so incensed by Kapoor's palette grab that he produced what he called the world's pinkest pink, which you can only buy on the express condition that Kapoor is not allowed to use your purchase.

Somehow Kapoor got his hands on some. Or rather, just the one finger – yes, that one – which he daubed in the pink paint, posting the result on Instagram. Semple is now working to put Kapoor in the shade by developing a new pigment to rival Vantablack.

Perhaps some of the materials engineers among our readers could find a way to make a true blacker-than-black of their own, and donate the gloomy pigment to the world?

THE pound sterling has shrunk in recent times, and Feedback doesn't just mean its drop in value against other currencies in the wake of Brexit. A new series of plastic banknotes are being introduced, which promise to be smaller, stronger and better able to survive a wash cycle (tumble dryers, on the other hand, appear to shrink them rather catastrophically).

Unfortunately, it turns out that the polymer notes incorporate traces of beef tallow, making them unfit for consumption by vegans and vegetarians, whose ire was aroused. The Bank of England says it will not be withdrawing the fatty notes from circulation, but will endeavour to replace the offending ingredient with coconut oil in future iterations.

Evidently caught off guard, the Bank frets in a report that "at the

same time, however, [we need] to understand whether the use of plant-based alternatives would raise its own concerns."

Those with an intolerance beware: from here on in, British banks may contain traces of nuts.

A FURTHER note on life cycles of urban clutter: Kate Belcher writes to inform us that we "have omitted an essential stage in describing the metamorphosis of unsecured bicycles (11 February); before turning into large mattresses, there is an intermediate stage when they have turned into shopping trolleys".

A MORE grounded take on where missing socks go: Brian Plowman writes that his 95-year-old grandmother is a keen collector of rainwater, maintaining water butts around her bungalow "wherever there's a sloping surface".



After mentioning the missing sock problem, Brian was told to use spare socks on the entry pipe for his own water butt, to stop moss and other detritus trickling in and creating an evil sludge at the bottom. The mucky stocking-filler can then be easily removed and the sock rinsed, or replaced entirely.

"Spookily enough, the regularity of finding single socks for the water butt has matched the level of receiving new socks each Christmas," says Brian.

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Driverless dynamics

In the UK's Lake District, tourists tend to drive slowly, leading to congestion on relatively long stretches of road. Would driverless cars make the flow dynamics better or worse? If any of the remaining drivers were scared of going close to the speed limit, would this negate the use of the driverless element?

■ The answer would depend on how automated vehicles were programmed to operate in varying circumstances. For example, they could be set up to drive more positively when traffic conditions are busy to help ease congestion, but adopt a more leisurely pace when traffic is light to let people view the scenery through which they are travelling. Freeing visitors from the task of driving could let them enjoy the Lake District or any scenic region more.

Vehicle occupants may also be less concerned about delays if they aren't driving, because they will be able to engage in other distractions such as watching a film, playing games or using social media – internet connectivity permitting.

UK research laboratory TRL, which works on the future of transport, is leading the GATEway Project in Greenwich, jointly funded by government and industry, to investigate the use, perception and acceptance of automated vehicles.

Traffic flow dynamics and adoption in urban and rural

environments are all important, and greater understanding will help industry and policy-makers understand the implications of driverless vehicles.

*Nick Reed
Academy Director, TRL
Wokingham, Berkshire, UK*

■ Driverless cars are unlikely to substantially speed up traffic in the Lake District, because most of the roads are single carriageway with little opportunity to overtake, and all traffic therefore has to drive at the speed of the slowest vehicle. And entrepreneurial tourist companies are likely to offer scenic tours at sedate speeds in driverless cars to those who can't or don't want to drive themselves.

If it is any consolation, many others experience traffic congestion, but without the wonderful scenery.

Where driverless cars could make a huge early impact is on congested motorways, where the outside lane could be reserved for driverless or driver-assisted cars running in close convoy at high speeds, passing vehicles in other lanes that are travelling slowly. Given the incentive of travelling at speed through congestion, this could lead to a rapid switch to driverless cars, and consequently increase the capacity of the motorway network.

Driving in close convoy in a single lane on a motorway should be one of the simplest tasks to automate, years before driverless vehicles are able to negotiate

London's Hyde Park Corner during the rush hour.

*Dave Neale
Truro, Cornwall, UK*

relativistic effects – is a matter of wild conjecture.

*Jon Richfield
Somerset West, South Africa*

Theoretically speaking

If Albert Einstein had never existed, presumably other physicists would have eventually developed the two relativity theorems. How quickly would they have done so if they'd had access to modern instrumentation?

■ Much modern instrumentation relies on concepts of Einsteinian relativity, so that speculation is possibly futile.

At the time, various experimental results had supplied so many hints to the theory of special relativity that Einstein worked it out rather quickly, producing his paper largely within 1905, and it is widely agreed that if he had not, then someone would have done so soon after.

But while the sophistication and creativity of special relativity was highly impressive, his theory of general relativity was on another level entirely, based on startling and enormously original insights. And yet it still took Einstein fewer than 10 years to produce.

How long it would have taken anyone else to derive, or even conceive, the theory – even given equipment equivalent to modern instrumentation to demonstrate

Round and about

People of my generation (I am 75) can remember when hens' eggs used to have a rounded end and a pointy end. Now the ends seem much more alike. Have eggs changed over the years, and if so, why? (Continued)

■ An earlier answer repeated some common misconceptions about how an egg is made and laid (14 January 2017). Eggshells are fully formed and hardened in the shell gland (uterus), where they spend about 20 hours. They do not emerge with soft shells that then quickly harden. Imagine the fun there would be on commercial farms, where eggs may be laid onto slatted wire, if they came out soft. In addition, if you are breeding millions of birds a year, nature occasionally cocks it up and there will be genetic faults, but it will not happen "frequently".

*Kim Critchley
Clarence Park, South Australia*

This week's question

SWIMMING SCHOOL

My Year 7 class and I have been trying to find out whether sharks can swim backwards. Can anyone settle the issue please?

*Simon Breare
York, UK*

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