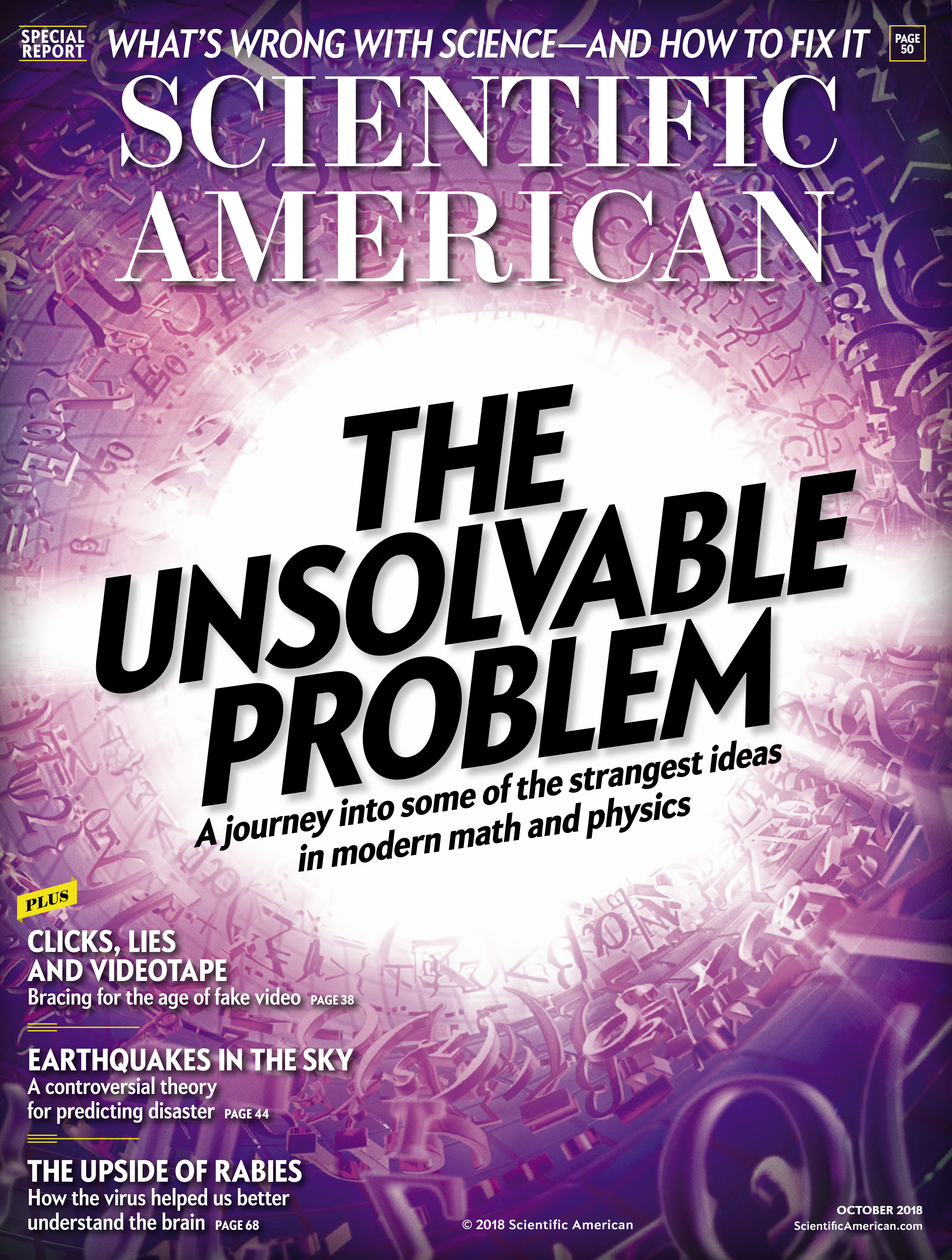

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SCIENTIFIC AMERICAN

THE UNSOLVABLE PROBLEM

A journey into some of the strangest ideas in modern math and physics

PLUS

CLICKS, LIES AND VIDEOTAPE
Bracing for the age of fake video PAGE 38

EARTHQUAKES IN THE SKY
A controversial theory for predicting disaster PAGE 44

THE UPSIDE OF RABIES
How the virus helped us better understand the brain PAGE 68

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so my cancer won't come back."
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Jessica / Breast Cancer Patient
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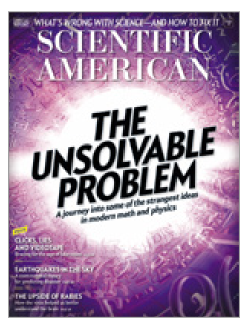
JABIN BOTSFORD *Getty Images (flooding in Houston, Tex.)*

ON THE COVER

Three mathematicians spent several years and 146 pages proving that the "spectral gap" problem—the question of whether materials have a gap between their lowest energy level and first excited state—is undecidable. To reach this conclusion, the researchers investigated the computer science of Turing machines, the mathematics of bathroom floor tiles and the foundations of quantum physics. Illustration by Mark Ross Studios.



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ON THE WEB

Forbidden Universes
Scientific American reports that the multitude of universes predicted by string theory may not exist after all, a suggestion that has sparked controversy among physicists.
Go to www.ScientificAmerican.com/oct2018/multiverse

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Mariette DiChristina is editor in chief of *Scientific American.* Follow her on Twitter @mdichristina

Proof of the Impossible?

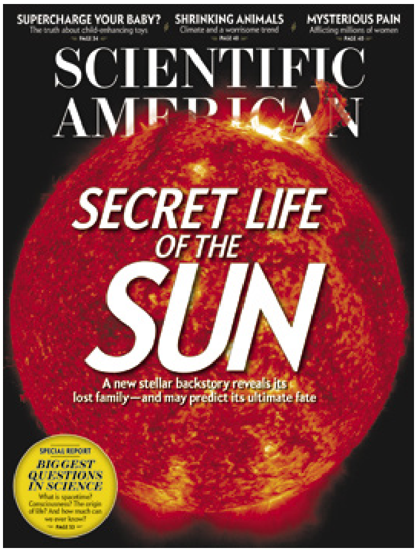
"This idea might seem obvious, but mathematics is about establishing concepts with absolute certainty," write Toby S. Cubitt, David Pérez-García and Michael Wolf in this issue's cover story, "The Unsolvable Problem." In their feature, they describe a mathematical odyssey to demonstrate the "undecidability"—that is, the unsolvable nature—of a certain problem in quantum physics. The journey takes them on a three-year "grand adventure," from a small town deep in the Austrian Alps into a world of complicated mathematics. The result was a 146-page proof and publication in the journal *Nature*. It all starts on page 28.

Several years ago a few different trips of my own—to Moscow, Doha (Qatar), Beijing and others—inspired the series "State of the World's Science." At the time, I was struck by how other countries looked to science and invested in it, with a variety of national goals. I decided that *Scientific American,* with 14 translated editions, should make a point of taking an annual look at this global enterprise.

In this year's special report, headed by senior editor Clara Moskowitz, we are looking at the challenges of research today. In "Make Research Reproducible," Shannon Palus examines the problem of reproducibility (*page 56*): a large percentage of scientific papers cannot be replicated by other researchers. The reasons can include multiple factors, such as imprecise methods, bad reagents and flaws in data collection. Starting on page 52, John P. A. Ioannidis writes about the ways we can "Rethink Funding," from not spending enough to properly financing the work in the first place to problems with the reward systems for individuals. He also outlines potential solutions. In "Help Young Scientists," beginning on page 62, Rebecca Boyle discusses the difficulties faced by individuals at the start of their career. Rounding out the section, in "Break Down Silos," Graham A. J. Worthy and Cherie L. Yestrebsky focus on interdisciplinary teamwork (*page 64*).

Elsewhere in the issue, you can discover how engineered forms of the rabies virus have provided new insights into the brain's inner workings (*page 68*); ponder a controversial theory that holds that the best early warnings of an earthquake could appear 180 miles above the ground (*page 44*); learn about new ways to evacuate in the event of a hurricane (*page 74*); and consider the all too disturbing reality of fake videos (*page 38*). As always, we hope that you enjoy making your way through the feature articles in this edition. We welcome your comments. SA

Illustration by Nick Higgins



June 2018

> **"It may not be a question of whether the universe is stranger than we understand but whether it is stranger than we *can* understand."**
>
> BARRY MALETZKY *PORTLAND, ORE.*

GRASP CEILING

In raising the question "How Much Can We Know?" [The Biggest Questions in Science], Marcelo Gleiser focuses on human consciousness and the extent to which we can "make sense of the world."

He misses the larger issue: our brains evolved to help us survive and reproduce, not to understand the cosmos. It may not be a question of whether the universe is stranger than we understand but whether it is stranger than we *can* understand.

BARRY MALETZKY *Portland, Ore.*

Gleiser exposes the limits of knowledge in the physical sciences. Kurt Gödel settled this subject in mathematics with his incompleteness theorems in 1931. Because the sciences are rooted in mathematics, it is only natural to include his work in any such discussion of epistemology.

AVERY CARR *Nesbit, Miss.*

GLEISER REPLIES: Regarding Maletzky's observation: It is indeed remarkable that brains that evolved to maximize our survival chances are able to write poetry, compose symphonies and prove theorems. Why this is so remains a mystery. It may well be that the universe is the puzzle we can't solve. It's hard to get out of the box when the box is everything that exists.

Gödel's incompleteness theorems did expose the limitations of mathematics as a self-contained logical process. I agree with Carr that his work must be included in a longer piece, which I did in my book The Island of Knowledge. *For this essay, space allowed me to focus only on the physical sciences.* [Editors' note: Read more about Gödel's incompleteness theorems in "The Unsolvable Problem," on page 28.]

GAME OF LIFE

Erik Vance's "Can You Supercharge Your Baby?" is a sensible article on the limitations of modern toys, videos and other paraphernalia in helping augment young children's mental development. Yet there is another aspect of child play he overlooks: the substitution of social games with "passive" toys used mostly alone, typically via a television, computer or cell phone, without exercise.

Social games are vital for the mental and physical development of children. Perhaps most important, such games are based on rules that are accepted by all players, and they are fun only if everybody abides by those rules. Children who play with cell phones can cheat at will; they are the masters of their digital universe and thus become self-centered, without consideration for resolving social conflicts.

EDUARDO KAUSEL
Massachusetts Institute of Technology

CONSCIOUS EXPERIENCE

Christof Koch's opening salvos against Daniel Dennett of Tufts University and like-minded philosophers in "What Is Consciousness?" [The Biggest Questions in Science] are misguided. Koch's basic argument is: (1) Dennett, motivated by the belief that we live in a "meaningless universe of matter and the void," denies that we have conscious experiences; (2) my toothache hurts; (3) ergo, Dennett is wrong.

Those who have read Dennett carefully should recognize the falsity of the initial premise. He understands fully the reality of pain. His goal is to encourage thinkers to exercise greater caution when theorizing about their own consciousness: given the human brain's complexity, it is to be expected that some of our casual intuitions regarding its operation may be misguided.

CHRISTOPHER TAYLOR *Madison, Wis.*

KOCH REPLIES: Dennett argues in his 1991 book Consciousness Explained *that people are terribly confused about consciousness. What they mean when they recount their experiences—for that is consciousness—is that they have certain beliefs about their mental states; each state has distinct functional properties with distinct behaviors. Once these outcomes are explained, there is nothing left to account for. Consciousness is all in the doing.*

He and others who take his eliminative materialist view of conscious experiences deny the existence of anything above and beyond associated behavioral dispositions and function. I find this position bizarrely incongruous with my lived experience. How is my back pain a belief and not an excruciating subjective state? Having spent many a wonderful dinner with Dennett, one of the most eloquent and knowledgeable philosophers I have encountered, I know that outside business hours, he acts like he has experiences like everyone else.

LIGHT AND DARK

"What Is Spacetime?" [The Biggest Questions in Science], George Musser's article on quantum gravity, makes me wonder if there are differences we can observe between the cases of dark matter falling into a black hole and normal matter doing so.

WONTAEK YOO *Pittsburgh*

I have long wondered why the speed of light exists. What is it and why is it so fundamental to physics? Musser presents the idea that atoms of space might undergo "phase transitions" and that black holes could be places where space "melts." It occurs to me that the speed of light could represent the melting point of spacetime.

ERIK EASON *Oregon City, Ore.*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MUSSER REPLIES: In answer to Yoo: Most physicists think that dark matter is a hitherto undetected but otherwise unexceptional type of particle, which would behave like ordinary matter, as far as black holes are concerned. Gravitation is a universal force that no matter is immune to. Although dark matter can fall into a black hole, it is less likely to do so because, if truly dark, it cannot lose energy by emitting light or dissipate momentum by friction and thus cannot readily spiral into a hole.

Regarding Eason's question: If spacetime does emerge from deeper ingredients, as I speculate in my article, the speed of light can no longer be taken as a given and will have to be explained. The answer is not yet known. In some scenarios, the speed of light arises from the dynamics of the building blocks of spacetime. Like the rest of the structure of the spacetime we observe, the speed of light is a property of one of the phases that theorists hypothesize. It loses meaning in the others. Think of the speed of surface waves in liquid water: the waves cease to exist in the water's solid and gaseous phases.

ERRATA

"A Painful Mystery," by Jena Pincott, should had referred to nearly 11 hours a week as 27 percent of a 40-hour workweek rather than 7 percent.

"What Are the Limits of Manipulating Nature?" by Neil Savage [The Biggest Questions in Science], incorrectly said that David Hsieh of the California Institute of Technology creates photoinduced superconductivity in a material called a Mott insulator that becomes insulating at very cold temperatures. Andrea Cavalleri of the Max Planck Institute for the Structure and Dynamics of Matter in Hamburg, Germany, and his colleagues found signs of photoinduced superconductivity in metals and insulators. Hsieh uses the same laser technique to induce unusual quantum effects in other materials.

Further, the article mistakenly referred to superconductors that must be cooled to within a few degrees of absolute zero as the only practical ones yet developed. While such superconductors have found more practical applications, those exhibiting superconductivity at much higher temperatures are widely used.

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Druggists Shouldn't Be Morality Police

Some states let them deny care for nonmedical reasons

By the Editors

In June, an Arizona woman was told by her doctor that her nine-week-old fetus had no heartbeat and that she was miscarrying. She was given a prescription for misoprostol, a drug that would help induce her body to clear the dead fetus. She went to a local Walgreens to get that medication, but the pharmacist there refused. Instead he told her she could return when he was not working or have her prescription passed along to another pharmacy. The woman said she was left explaining in front of her seven-year-old and other customers that she had wanted to have a baby but that there was no heartbeat. Yet she was still refused the medication.

In Arizona and at least six other U.S. states, pharmacists have the legal right to refuse to fill emergency contraception prescriptions—not for medical reasons but simply based on moral grounds. In such cases, the law allows druggists in Arizona, Arkansas, Georgia, Idaho, Mississippi, South Dakota and Texas to override the judgment of physicians.

This puts patients at risk—primarily women, because moral qualms nearly always have to do with birth control or with so-called abortion pills. But there are many reasons other than birth control that a woman might take contraceptives, ranging from regulating menstrual cycles to helping manage endometriosis or polycystic ovarian syndrome. Failure to obtain legitimately prescribed drugs could result in significant pain or other medical complications, in addition to the obvious risk of unwanted pregnancy. But in these states, pharmacies and pharmacists can just say no.

Such policies are a particular problem in rural parts of the country where drugstores may be located very far apart, forcing people to travel significant distances to find a cooperative pharmacist. There are no official tallies on how often such incidents occur, although some anecdotal examples of such arbitrary refusals are chilling. In January 2007, for example, a 23-year-old mother in central Ohio went to her local Walmart for emergency contraception.

According to the National Women's Law Center, the pharmacist on staff "shook his head and laughed" and told her that no one there would sell her the medication even though the store had it in stock. As a result, she had to drive 45 miles to find another pharmacy that would provide her with the drug. This woman's experience is particularly worrisome because delays taking emergency birth-control medication can increase the odds of pregnancy.

In states with "conscience carve-outs" for druggists, pharmacies honoring those policies should be required to preemptively notify state authorities and medical providers that they might refuse service. That way, women and their doctors could make alternative arrangements to fill prescriptions at pharmacies that will give them the medications they need—avoiding situations such as the recent one in Arizona. This follows a model worked out in 2014, when the U.S. Supreme Court told the Obama administration that certain employers with religious objections did not have to offer an insurance plan with birth-control coverage. But these employers did have to notify the Department of Health and Human Services so the government and insurers could provide birth-control coverage via a private insurance plan or a government-sponsored one. (The Trump administration has since complicated this approach and scrapped government notification requirements.)

And in situations where individual pharmacists may refuse service—even if their pharmacies generally fill family-planning prescriptions—there should be a legal requirement to automatically refer that prescription to another pharmacy within a certain reasonable distance or to have a backup druggist on call to do the work so that patients can get medications quickly and efficiently.

Pharmacists play a vital role in the health care system: helping patients treat illnesses, maintain their health, educating them about drug interactions and answering questions. But these professionals are hurting people—especially women—when they force them to go hunting for a place to fill a prescription. SA

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Illustration by Samantha Mash

GENE THERAPY POISED FOR IMPACT ON CHILDHOOD DISEASES

A conversation with **KEVIN FLANIGAN**, MD, director, Center for Gene Therapy, Nationwide Children's Hospital

Nationwide Children's Hospital, in Columbus, OH, cares for children from around the world. Its research institute is among the top 10 free-standing children's hospitals in terms of National Institutes of Health funding. Its Center for Gene Therapy develops treatments for a variety of childhood disorders, particularly neuromuscular and neurodegenerative diseases, and collaborates with pharmaceutical companies to move potential therapies into clinical trials.

What is the state of the art of gene therapy today?

After more than 20 years of research into gene transfer, it is finally reaching the clinic in a meaningful way. Part of this is based on the increasingly successful development of the viral vector systems we now use, adeno-associated viruses (AAVs), which have become the workhorses for gene therapy. After many years of preclinical research with AAV vectors, gene therapies for many single-gene disorders are now in clinical trials. Some have already shown extraordinary promise for changing the disease course for devastating childhood illnesses.

What success have you had in developing therapies?

The most striking published result so far has been in gene transfer of the SMN1 gene into patients with spinal muscular atrophy type 1, where the first human trial showed a dramatic improvement in outcomes. This devastating disorder affects the motor neurons, and typically causes death or the need for mechanical ventilation by the age of two years. Using a vector developed by Brian Kaspar in his lab at Nationwide Children's, Jerry Mendell's team treated 15 patients with systemic delivery of an AAV9 vector carrying the SMN gene. They showed it was safe, but more strikingly, all of the patients were alive or without mechanical ventilation at age 20 months, as compared to only the 8% expected based upon natural history studies. This is really quite a dramatic change in the clinical course, and has the potential to change treatment of the disease around the world.

What other diseases are you tackling?

We have trials under way for Duchenne muscular dystrophy, which affects about 1 in 5200 boys. These trials include gene transfer of micro-dystrophin, miniaturized to fit into an AAV capsid, as well as a surrogate gene (GALGT2) that can in some ways substitute for the missing protein. We have trials under way or planned for some forms of limb-girdle muscular dystrophy and Charcot-Marie-Tooth disease, and ongoing preclinical projects addressing facioscapulohumeral muscular dystrophy, myotonic dystrophy type 1, and a variety of other neuromuscular disorders. In addition, we have trials under way for other diseases that primarily affect the central nervous system, such as Sanfilippo syndrome (or mucopolysaccharidosis type 3) and Batten disease.

Why do you emphasize childhood neuromuscular diseases?

Most importantly, many childhood neuromuscular diseases are absolutely devastating disorders for which no other therapy is available. I have studied these diseases for 25 years, and my colleague Jerry Mendell has worked on them for more than 50 years, so we know this patient population well. We have viruses that are taken up by skeletal muscle quite well, and we can biopsy muscle to directly evaluate how our viral payloads are expressed, which is very helpful. We also have an excellent clinical research team that continues to develop and validate appropriate functional outcomes in these diseases, which is necessary for good clinical trials.

Could you move into treating other diseases?

The lessons learned from preclinical and clinical studies with vectors for neuromuscular diseases are applicable to many other diseases. We don't expect these approaches will work only for neuromuscular diseases, but that's where our areas of interest have historically been, and these studies have allowed us to demonstrate proof of concept in human safety and efficacy. As I mentioned earlier, we have programs directed toward the central nervous system as well. We've gained a lot of experience in navigating the regulatory process. We have an in-house regulatory group, and it's one of the reasons that we've submitted more than 15 active gene therapy Investigational New Drug applications. We will have multiple new INDs coming out within the next year.

How does gene therapy fit with pediatric medicine?

Many pediatric disorders are devastating or lethal, which makes the argument for starting with these most severe diseases. One advantage in pediatric medicine is that one of the great challenges of gene therapy is manufacturing sufficient quantities of any viral vector. Since many of these therapies dose by weight, using a given number of virus particles per kilogram, we can test them more readily in pediatric diseases, and can design trials that involve more patients.

Are you optimistic that gene therapy will reach the clinic?

I am very optimistic. One sign that it's moving toward practice is the number of biopharmaceutical companies that are now developing gene therapies. Some of these are companies that we have partnered with, but regardless of whether we consider products licensed from Nationwide Children's or elsewhere, the enthusiastic and growing engagement of biopharma partners signals great confidence in the field.

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Joseph Gogos is a neuroscientist at the Zuckerman Institute at Columbia University.

New Drugs from Old

Repurposing medications could let us treat intractable illnesses

By Joseph Gogos

Despite decades of research, disorders of the brain have proved especially difficult to treat. Consider Alzheimer's disease. To date, every single clinical trial of a treatment for Alzheimer's has failed to halt its progress. In January, Pfizer announced that it had ended research on drugs for it, as well as for Parkinson's disease. Autism has been similarly frustrating. Then there is schizophrenia, which has not seen a breakthrough for more than 60 years, since the discovery of chlorpromazine (brand name: Thorazine)—which happened largely by chance.

But the story of chlorpromazine offers a powerful lesson: originally an antihistamine, it was repurposed as an antianxiety medication. That led to doctors trying it in people with pathological anxiety and in agitated psychotic patients. Finally, with a few modifications, it was reborn as an antipsychotic, ushering in a generation of medications to treat a variety of psychiatric disorders, from schizophrenia and bipolar disorder to severe depression and anxiety. These are not miracle cures, and they have serious side effects—but they are far better than what existed before.

As a neuroscientist who has studied schizophrenia for decades, I am convinced that we could have similar successes with other medicines already on our shelves, which may hold untapped promise for treating brain diseases—if only pharmaceutical companies can be prompted to share their data with scientists. Because an existing drug has already passed FDA tests to prove it is nontoxic to humans, successfully repurposing it could take less than half of the estimated 13 years and significantly less than the average $2-billion to $3-billion cost of developing a single drug from scratch. The thousands of FDA-approved drugs thus represent a vast resource that can potentially be modified to target any number of conditions. But this potential is largely unexplored, in part because companies focus on specific diseases and would have to restructure their R&D programs to look at others.

There are also thousands of drugs that are *not* FDA-approved, such as those stalled in clinical trials or discontinued by drugmakers. When a company abandons development of a drug, whatever researchers know is locked up in that company's files and might as well be lost. Scientists need access to this information, and we need it now. Starting in the early 2010s, the U.S. National Institutes of Health and the U.K.'s Medical Research Council have been striking deals to take abandoned drugs from their pipelines and release that information publicly. The NIH's National Center for Advancing Translational Sciences even provides a legal framework that lets companies protect their interests while sharing drug data. Other initiatives to create similar databases of approved and failed drugs are also under way.

If this information could be funneled into a centralized resource, along with existing data on approved drugs—and combined with the explosion in genetic knowledge related to the underlying disease mechanisms—it would be a revelation. Researchers could employ the latest tools in bioinformatics, data science and machine learning to uncover common molecular themes among or between diseases and potential drugs.

Ultimately the key is access, but many pharmaceutical companies are still reluctant to reveal anything that might jeopardize their intellectual property. Even academics may hesitate to share with competing laboratories. To remedy this, the FDA and similar entities must develop incentives for sharing data, such as by creating legal safeguards for privacy and commercial interests. These incentives could then open the floodgates for easy-to-use, open platforms for efficiently sharing and mining data. This would not have been possible five years ago. But now is a pivotal moment, and we have never been closer to real breakthroughs.

In my lab, we are testing certain cancer drugs that restore some of the biological processes that are disrupted in schizophrenia. We want to see if the drugs have the same restorative properties in the brain cells of schizophrenia patients. This is a proof of concept for the idea that a systematic and strategic approach to drug repurposing could actually move the needle. There is no time to waste. We now have the capabilities to deploy a legion of virtual researchers in search of these eureka moments. What we need is cooperation from drug companies and academic scientists alike—and access to the lifesaving data they hold. SA

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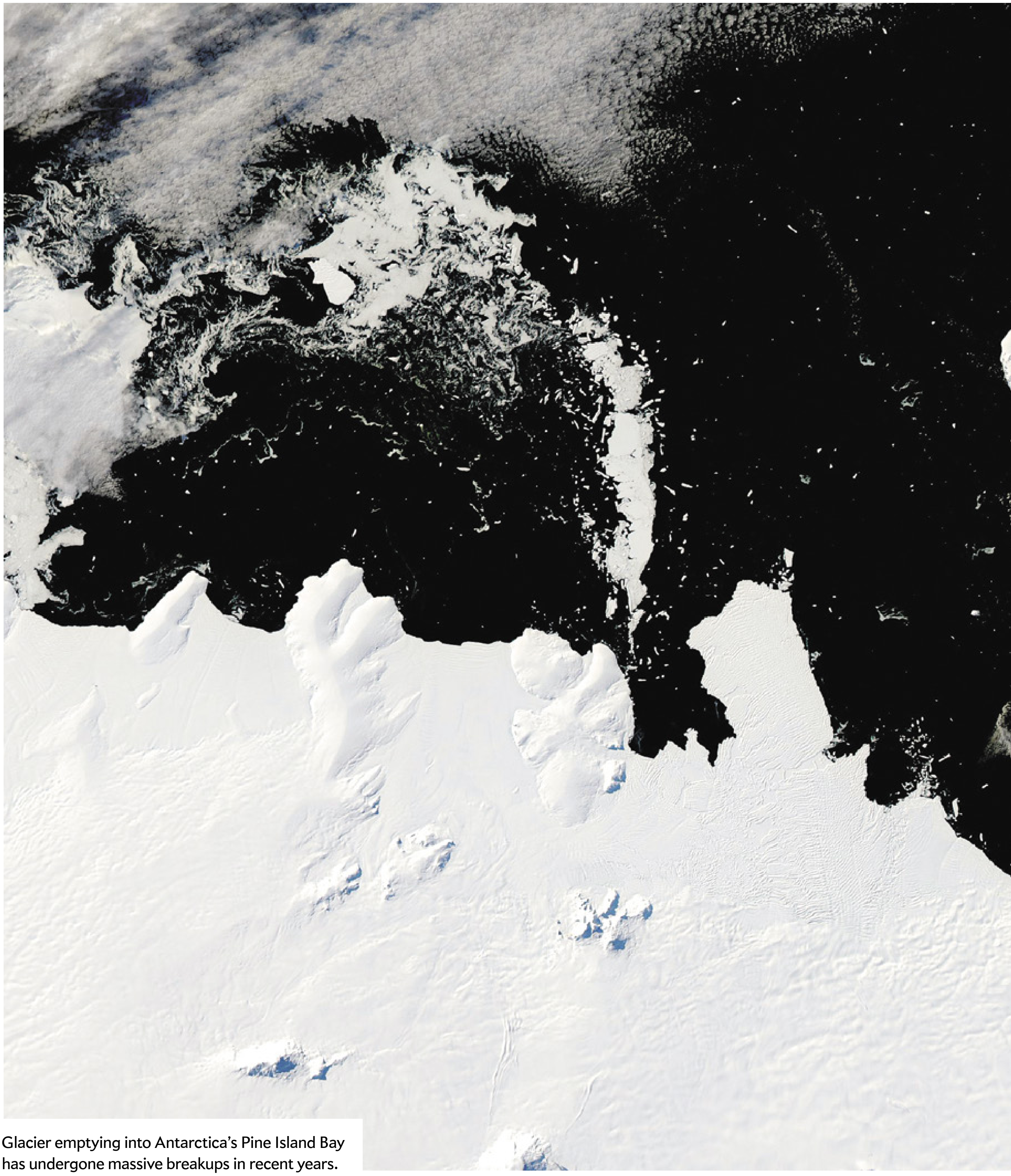
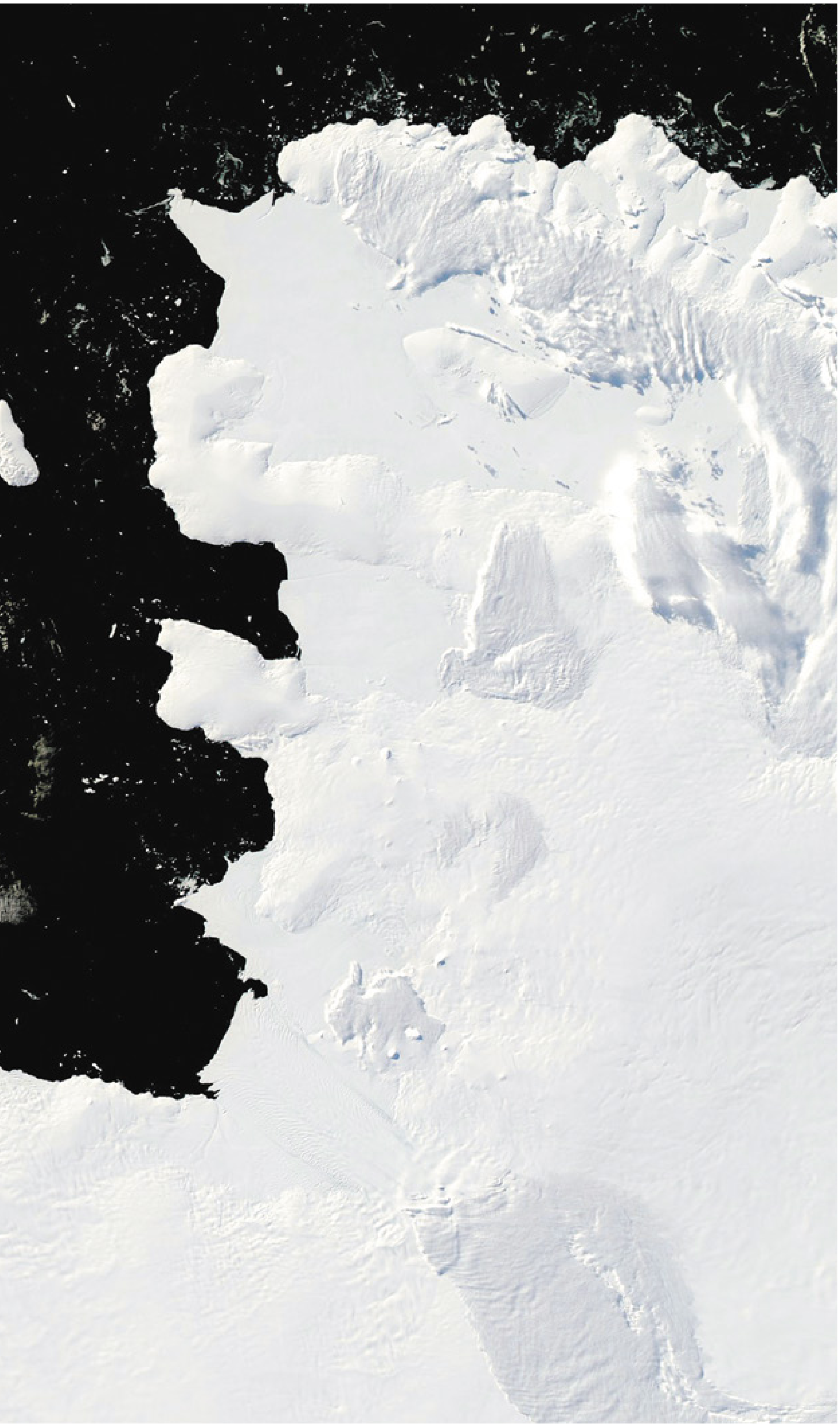
Illustration by Jori Bolton

ADVANCES



Glacier emptying into Antarctica's Pine Island Bay has undergone massive breakups in recent years.



ALAMY

INSIDE

CLIMATE SCIENCE

Slippery Slope

Seafloor maps reveal Antarctic glacier had a bumpy ride

Antarctica's Pine Island Glacier holds a dubious honor—it is currently the largest Antarctic contributor to global sea-level rise, thanks to the enormous amount of ice it has lost in recent decades. Now scientists have identified the likely cause of some of the glacier's most spectacular calving events, which have birthed icebergs several times the size of Manhattan.

The culprit: submerged rock ridges that poke up high enough to occasionally hit the bottom of the glacier. This activity creates small cracks that grow and eventually cause massive chunks of ice to break off. But the undersea rocks are not all bad news—they can also help stabilize the glacier by grinding against its underside, buttressing it against flowing faster out to sea.

Jan Erik Arndt, a geophysicist at the Alfred Wegener Institute Helmholtz Center for Polar and Marine Research in Germany, and his colleagues departed Punta Arenas, Chile, in February 2017 onboard the icebreaker *Polarstern*. A week or so later they arrived in Pine Island Bay, an inlet filled with icebergs and dominated by the glacier's 40-meter-high face. They were there to figure out what controlled the stability of this expanse of ice.

Arndt and his colleagues launched sound waves from the *Polarstern*'s hull into the near-freezing water. By measuring how long it took the waves to bounce off the seafloor and return to the ship, the team mapped hundreds of square kilometers of the bay's underwater topography. The researchers focused on an area exposed by the glacier's recent calving—a swath of seafloor that used to lie below about 400 meters of ice. "It was a good opportunity to go in there and map this area that was not accessible before," Arndt says.

He and his team discovered a complex undersea landscape. One feature literally stood out—a rocky outcropping that, at its tallest point, reached within 375 meters of the surface. "We were surprised to see this huge ridge," Arndt says. This rock, the team realized, had very likely pushed against the bottom of Pine Island Glacier in the past. The giveaway was a bump on the glacier's surface—glaciologists call it a "rumple"—directly above the location of the ridge in archival satellite images. "We saw the surface imprint of the topography underneath on the ice shelf," Arndt explains. As the ice pressed against the ridge, it probably also acted as a brake, preventing the glacier from flowing unimpeded into the ocean, the researchers hypothesize. They suspect it had been effectively pinned that way since the 1940s.

But the brake eventually failed; Pine Island Glacier probably lost contact with the ridge in 2006, after a warmer current of water eroded the glacier's underside. That is when the rumple disappeared in satellite images, the team reported in June in the *Cryosphere*. (Scientists say a volcano under the glacier, discovered earlier this year, most likely contributes to its thinning as well.) As Pine Island Glacier once again slid toward the sea, it probably hit other submerged rock features the *Polarstern*'s mapping identified, the researchers say. Those collisions stressed the ice, creating kilometer-long rifts spotted in images taken in 2007 and 2011. These rifts then grew, finally spawning giant icebergs.

Seafloor features are "really important" to an ice shelf's stability, says Richard Alley, a geoscientist at Pennsylvania State University, who was not involved in the research. This study is "addressing an interesting question in a fascinating place," Alley says. Jeremy Bassis, a glaciologist at the University of Michigan, adds: "The troughs and bumps in the bottom of the ocean beneath the ice play a huge role in regulating when the ice will break."

As glaciers flow into the sea and melt, sea levels rise. That is bad news for a large chunk of the world's population; roughly 40 percent of all people live within 100 kilometers of a coastline. Some U.S. cities, such as New Orleans, already lie below sea level. Others, including Miami, currently experience regular flooding.

For now, Pine Island Glacier is stable—its northern section is pinned by a small hill on land, and its southern front is corralled by a thick stream of ice. But change is on the way, Arndt and his colleagues predict. Late last year they spotted a 30-kilometer-long rift in the glacier—the likely site of its next calving event.

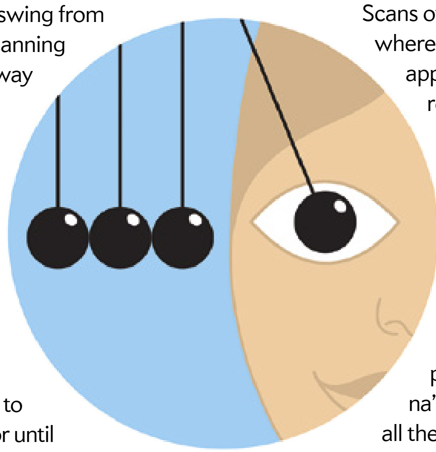
—*Katherine Kornei*

COGNITIVE SCIENCE

Seeing Blind

A visually impaired woman can still perceive motion

Milena Canning can see steam rising from a coffee cup but not the cup. She can see her daughter's ponytail swing from side to side, but she can't see her daughter. Canning is blind, yet moving objects somehow find a way into her perception. Scientists studying her condition say it could reveal secrets about how humans process vision in general.



Canning was 29 when a stroke destroyed her entire occipital lobe, the brain region housing the visual system. The event left her sightless, but one day she saw a flash of light from a metallic gift bag next to her. Her doctors told her she was hallucinating. Nevertheless, "I thought there must be something happening within my brain [allowing me to see]," she says. She went from doctor to doctor until she met Gordon Dutton, an ophthalmologist in Glasgow, Scotland. Dutton had encountered this mystery before—in a 1917 paper by neurologist George Riddoch describing brain-injured World War I soldiers. To help enhance Canning's motion-based vision, Dutton prescribed her a rocking chair.

Canning is one of a handful of people who have been diagnosed with the "Riddoch phenomenon," the ability to perceive motion while blind to other visual stimuli. Jody Culham, a neuroscientist at Western University in Ontario, and her colleagues launched a 10-year investigation into Canning's remarkable vision and published the results online in May in *Neuropsychologia*. The team confirmed that Canning was able to detect motion and its direction. She could see a hand moving toward her, but she could not tell a thumbs-up from a thumbs-down. She was also able to navigate around obstacles, reach and grasp, and catch a ball thrown at her.

Scans of Canning's head showed an apple-sized hole where the visual cortex should be. But the lesion apparently spared the brain's motion-processing region, the middle temporal (MT) visual area. "All the credit [for Canning's perception] must go to an intact MT," says Beatrice de Gelder, a neuroscientist at Maastricht University in the Netherlands, who was not involved in the study.

The next mystery is how information from the eyes gets to the MT without traveling through the visual cortex. "I think of the primary visual pathway as a highway. In Milena's case, the highway dead-ends, but there are all these side roads that go to the MT," Culham says. "It's got to be one of these indirect routes, but we are not yet sure which one." These side roads most likely exist in all our brains as remnants of the early visual system that evolved to detect approaching threats even without full-fledged sight, Culham says.

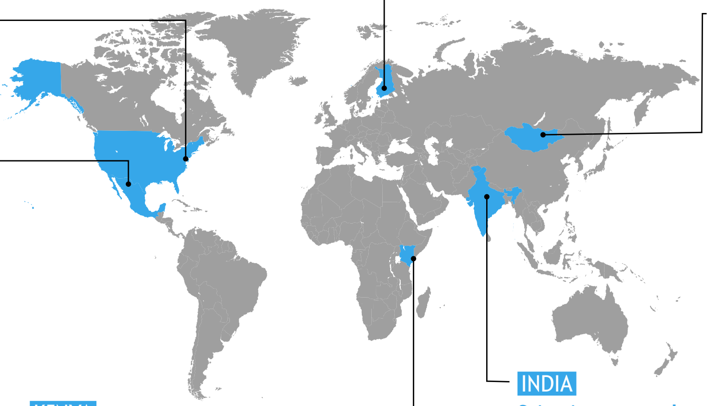
Canning is an eager participant in the researchers' ongoing study. "If I can help them understand the brain more," she says, "I could understand why I'm seeing what I'm seeing." —*Bahar Gholipour*

Illustration by Thomas Fuchs

IN THE NEWS

Quick Hits

By Maya Miller



U.S.

A first-of-its-kind lawsuit claiming that the federal government's actions caused climate change is moving forward. The U.S. Supreme Court dismissed an attempt by the Trump administration to halt the lawsuit, filed by young plaintiffs in Oregon.

FINLAND

About 10,000 years ago humans lived in settlements in a part of southern Finland that is now under several meters of lake water, researchers found. A team of archaeologists and marine experts dove deep into the lake to find what are now the earliest known signs of human habitation in the region.

MEXICO

A Mexico City–based social enterprise is providing computer programming training to teenagers deported from the U.S. The organization, Hola<code/>, is offering five-month software engineering "boot camps" in a bid to give the young deportees employable skills and ultimately boost the nation's technology sector.

MONGOLIA

People were performing dentistry on horses on the vast grasslands of the Mongolian steppe roughly 3,000 years ago, according to a research team's findings. The study suggests nomads there were some of the first humans to use the animals for wide-scale transport, spurring the early beginnings of globalization.

KENYA

Nairobi, a city with some of the world's worst traffic, is planning to implement car-free Wednesdays and Saturdays in two of its most congested areas. Policy makers hope this will encourage public transportation use and reduce air pollution.

INDIA

Scientists wrote a letter to the Indian president to voice concerns over alleged political attacks on science. The letter criticized the government's decision to transfer a senior scientist to a less influential post after he complained about moves to privatize parts of the nation's central space agency.

For more details, visit www.ScientificAmerican.com/oct2018/advances

ANIMAL PHYSIOLOGY

Flock Immunity

Birds' ability to fight germs depends on migration patterns

Meadow pipit

As autumn slides into winter every year, many birds in Europe and Asia pack up and fly south to bask in the tropical African sunshine. When spring rolls around, they return to the temperate Palearctic zone to mate and raise their offspring. Researchers wanted to know why these long-distance fliers do not get travelers' flu.

"When we go abroad on holiday, we need all sorts of vaccinations," says Emily O'Connor, an ecologist at Lund University in Sweden. "But birds don't have the option of pharmaceutical protection. It puzzled us: How is it they can cope so well with something so difficult for us to cope with?"

To find out, O'Connor and her colleagues classified more than 1,300 songbird species as migratory, sedentary African or sedentary Palearctic—an example of the last is the meadow pipit (*shown*). They then trapped wild birds from a representative subset of 32 species, taking blood samples for genetic analysis. The researchers were looking for genes that encode a class of immune system proteins called MHC-I, which are involved in recognizing pathogens. The greater the number of such genes, the more kinds of invaders an animal's immune system can detect, O'Connor says.

By this measure, sedentary African birds had the most robust immune systems. Because most Palearctic birds first evolved in the tropics and later spread northward, the researchers suspect these species developed less MHC-I diversity. The results were published in May in *Nature Ecology & Evolution*.

"Migratory birds, because of the lifestyles they have, have to deal with two separate sets of pathogens," O'Connor says. "I was expecting them to have the highest gene diversity of all the groups, so I was really surprised to find it was really similar to [that of] the European birds."

Young birds are most susceptible to pathogens just after hatching, and the stress of reproduction makes their parents more likely to get sick then, too. For both reasons, O'Connor suspects that evolution may have pushed migratory species to favor genes associated with resistance to pathogens common in the north, where they are born, at the expense of those that protect against tropical germs.

Alternatively, migratory species may have invested in other forms of immunity that are not pathogen-specific, says University of Exeter evolutionary biologist Camille Bonneaud, who was not involved in the study. "We now need to further explore whether migratory species invest less in fighting pathogens," Bonneaud says, and "more in other types of immune processes."

—*Jason G. Goldman*

ABI WARNER *Getty Images*

BIOLOGY

Body Balance

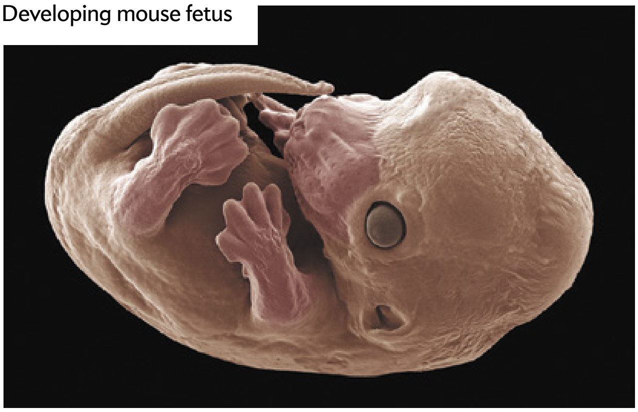
How different limbs grow at the same rate during development

Species with symmetrical body plans have been roaming the earth for about 400 million years. Human beings have long shown an intense interest in this property in our own species—take the importance of symmetry in perceptions of beauty or the famous depiction of the outstretched human body in Leonardo da Vinci's *Vitruvian Man.*

Now scientists have gone a step further. Alberto Roselló-Díez, a developmental biologist currently at the Australian Regenerative Medicine Institute at Monash University, led a study of how a mouse fetus maintains symmetry as it develops. By making one of the fetus's limbs grow more slowly than the other, the team observed how cells communicate to ultimately correct the asymmetry. No study had successfully examined this phenomenon until now.

After a year of failed attempts, Roselló-Díez and his team created a model in mice. Borrowing a technique previously developed for modifying cells in a laboratory dish, the researchers injected into the mouse fetus's left hind leg a type of cell that restricted the leg's growth. They found that the cells surrounding the suppressed tissue communicated with the placenta, which then signaled the rest of the organism's tissues—including the other hind leg—to slow their growth until the hindered limb caught up. Then, uniform growth resumed. The findings were published in June in *PLOS Biology.*

Developing mouse fetus



Think of this process as a "three-legged race," says Kim Cooper, a cell and developmental biologist at the University of California, San Diego, who was not involved in the study. "If one person is going faster, it's harder to stay in sync. This placenta mechanism makes it possible for the slower one to catch up," Cooper says.

The study offers insight into limb development and so-called catch-up growth. But the research also raises new questions: for example, once the limb has reached the same level of growth, how does the other limb know to start growing again? "We kind of expect symmetry in our limbs," says Adrian Halme, a cell biologist at the University of Virginia, who was also not involved with the study. "But how they achieve that symmetry is really striking."

—*Maya Miller*

STEVE GSCHMEISSNER *Science Source*

NEUROSCIENCE

Brain Bar Codes

New technique lets scientists map the organ in unprecedented detail

Neuroscientists know a lot about how individual neurons operate but remarkably little about how large numbers of them work together to produce thoughts, feelings and behavior. They need a wiring diagram for the brain—known as a connectome—to identify the circuits that underlie the organ's functions.

Now researchers at Cold Spring Harbor Laboratory and their colleagues have developed an innovative brain-mapping technique and used it to trace the connections emanating from nearly 600 neurons in a mouse brain's main visual area in just three weeks. This technology could someday be used to help understand disorders thought to involve atypical brain wiring, such as autism or schizophrenia.

The technique works by tagging cells with genetic "bar codes." Researchers inject viruses into mice brains, where the viruses direct cells to produce random 30-letter RNA sequences (consisting of the nucleotide "letters" G, A, U and C). The cells also create a protein that binds to these RNA bar codes and drags them the length of each neuron's output wire, or axon. The researchers later dissect the mice brains into target regions and sequence the cells in each area, enabling them to determine which tagged neurons are connected to which regions.

The team found that neurons in a mouse's primary visual cortex typically send outputs to multiple other visual areas. It also discovered that most cells fall into six distinct groups based on which regions—and how many of them—they connect to. This finding suggests there are subtypes of neurons in a mouse's primary visual cortex that perform different functions. "Because we have so many neurons, we can do statistics and start understanding the patterns we see," says Cold Spring Harbor's Justus Kebschull, co-lead author of the study, which was published in April in *Nature.*

The bar-coding method represents a major leap for connectome mapping. With just 30 nucleotides, a researcher can generate more unique sequences than there are neurons in the brain, says neuroscientist Botond Roska of the Institute of Molecular and Clinical Ophthalmology Basel in Switzerland, who was not involved in the work: "I predict that as this technology matures, it will be a key way we analyze brain connectivity." —*Simon Makin*

Representative Bill Foster of Illinois, a former physicist.

SCIENCE POLICY

A Conversation with the Only Physicist in Congress

Representative Bill Foster weighs in on the most important science issues facing the country

Before being elected to Congress in 2008, Bill Foster, a Democrat, worked for more than 20 years as a physicist at Fermi National Accelerator Laboratory in Batavia, Ill. Now, as one of a handful of members of Congress with a Ph.D. in science, he says there is an urgent need for more scientists in politics. At least eight candidates with science backgrounds—though not necessarily doctorates—will be on the ballot for seats in the House or Senate in November. Foster sat down with SCIENTIFIC AMERICAN to discuss science's role on Capitol Hill amid the current divisive political climate. An edited excerpt of the conversation follows.

—*Dina Fine Maron*

How does it feel to be one of the only scientists in Congress?
Lonely. I was actually the third Ph.D. physicist when I came to Congress. We had then Representative Rush Holt of New Jersey (a Democrat), who is now running the American Association for the Advancement of Science, and the late Representative Vern Ehlers of Michigan—a very moderate Republican and a thoughtful guy. We still have a Ph.D. in mathematics, Representative Jerry McNerney of California (a Democrat). But in terms of physics, chemistry, et cetera, I'm all that's left.

Does this background affect your role as a politician?
Almost every issue that comes up has a technological edge to it. For example, with the Iran nuclear deal, I found that members of Congress—both Democrats and Republicans—would just come to me, asking me to serve as an interpreter on the purely technical aspects of it. There's only one of me, and there are 434 other members of the House, so I simply couldn't provide the diffusion of technical knowledge that is missing here. I spent a long time in classified briefings with the experts at the weapons labs and asked all the "What if" questions and "Would we be able to detect something under the agreement?" Then I had to translate all that technical information.

Does partisan politics limit your ability to raise scientific issues?
In a typical hearing of the House Committee on Science, Space, and Technology or Financial Services Committee—both of which I am on—you will get three Republican witnesses and a single Democrat. These committee policies are largely at the discretion of the chairman. When you look at simple reforms that would make [Congress] work in a more bipartisan, fact-based way, just having an equal number of witnesses from both sides would be a real step forward. I think it's incumbent on us, if the Democrats do take over again, that we go out of our way to make sure the rules are not so winner-takes-all.

Politics is very different from science—in science, if you stand up and say something that you know is not true, it is a career-ending move. It used to be that way in politics. It has taken me a while to adjust to politics where, for many who practice it, the question is not "Is it true?" but "What can I convince the voting public is true?" That psychology has bled into politics more than it should.

What is the most important science-related issue now facing Congress?
Aside from evidence-based political debate, I think it is understanding that technology is changing our society, our country and our world at an unprecedented rate. It has already upended labor markets. We should have a dedicated tech committee. I think there are six or seven House committees that claim they are doing information technology. We should consolidate tech and get a core competence in that.

What are some of your specific technology concerns?
If the U.S. started issuing digital cash [meaning virtual currency that would pass between individuals with no transaction fee], immediately people would use that instead of credit cards. That would affect a huge source of revenue for banks large and small. Other countries are already moving in that direction. And if we just say, "No, we're going to stick with our way of doing things"—and the European Union starts issuing digital euros, for example—you would find that the whole world will just walk away from the U.S. dollar. I don't think that's a recipe for making American finance great again.

TOM WILLIAMS *Getty Images*

ASTROBIOLOGY

Missing E.T.

Ancient Earth's atmosphere raises questions in the search for extraterrestrial life

Take a deep breath. About 20 percent of the air that just moved through your mouth or nostrils is oxygen—the gas much of life on Earth needs to survive. If you had taken that breath about 1.87 billion years ago, however, you would have croaked.

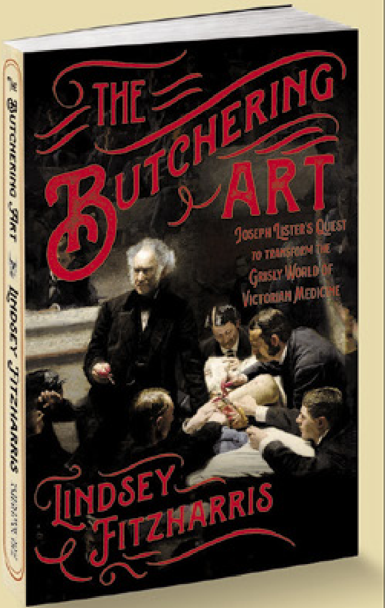
Until recently, little was known about oxygen's abundance in the atmosphere back then, when microbes were the only life on the planet. Now geologists doing fieldwork in northern Canada have confirmed for the first time that oxygen was extremely scarce.

The fact that life flourished amid such low oxygen levels presents a problem for scientists hunting for extraterrestrial life. The presence of the gas in the atmosphere of a planet is considered a telltale sign that it could harbor life, explains Noah Planavsky, a biogeochemist at Yale University and a co-author of the new study, published in July in the *Proceedings of the National Academy of Sciences USA*. But if environments with extremely low oxygen concentrations can still support life, space telescopes designed to detect an abundance of the gas may never find such life. "Even [if such planets are] teeming with complex life, they may appear—from a remote detectability point of view—as dead planets," Planavsky says.

Planavsky and his team tested rocks for concentrations of the element cerium, which serves as a proxy for ancient oxygen levels. Oxygen binds to cerium in seawater and removes it, leaving less cerium behind to be deposited in sedimentary rock. The measured cerium levels correspond to oxygen concentrations of about 0.1 percent of present atmospheric levels, the team reported.

Such hard data, Planavsky says, should help inform the construction of the next generation of telescopes designed to hunt for life on other worlds. Those currently in the works—such as NASA's James Webb Space Telescope (JWST)—cannot detect oxygen at such low concentrations, says Edward Schwieterman, an astrobiologist at the University of California, Riverside, who was not involved in the work.

Future space telescope missions may be better able to detect low oxygen concentrations. For now, researchers scanning the night sky for E.T. should not hold their breath. —*Lucas Joel*



SPORTS MEDICINE

Heading Off Injury

Female soccer players are more vulnerable to brain damage than males are

Repeatedly heading a soccer ball exacts a toll on an athlete's brain. But this cost—measured by the volume of brain cells damaged—is five times greater for women than for men, new research suggests.

The study provides a biological explanation for why women report more severe symptoms and longer recovery times than men following brain injuries in sports. Previously some researchers had dismissed female players' complaints because there was little physiological evidence for the disparity, says Michael Lipton, a neuroscientist at the Albert Einstein College of Medicine and a co-author of the paper.

Lipton's team used magnetic resonance imaging to peer into the skulls of 98 adult amateur soccer players—half of them female and half male—who headed the ball with varying frequency during the prior year. For women, eight of the brain's signal-carrying white matter regions showed structural deterioration, compared with just three such regions in men (damage increased with the number of reported headers). Furthermore, female athletes in the study suffered damage to an average of about 2,100 cubic millimeters of brain tissue, compared with an average of just 400 cubic millimeters in the male athletes.

Lipton does not yet know the cause of these sex differences, but he notes two possibilities. Women may suffer stronger whiplash from a cranial blow because they generally have less muscle mass than men to stabilize the neck and skull. Alternatively, a dip in progesterone, a hormone that protects against swelling in the brain, could heighten women's vulnerability to brain injury during certain phases of their menstrual cycle.

Thomas Kaminski, a sports physiologist at the University of Delaware, who was not involved in the work, calls it "truly groundbreaking." The research is unique in highlighting the cumulative effect of repetitive knocks on the skull, as opposed to major traumatic injuries, he says. "Very few of these subjects had a history of concussion."

Researchers are now eager to determine if these white matter changes carry long-term cognitive consequences. Until more is known, Kaminski advocates a proactive approach to limiting the damage caused by headers. In August he met with U.S. Soccer Federation officials to craft science-based guidelines for practicing the move in youth leagues.

Carla Garcia, a participant in Lipton's study, says that after 47 years of playing soccer, she has no plans to quit using her head. But she notes, "If there's any way we can make the sport safer for children, that's important." —*Daniel Ackerman*

ERIK ISAKSON *Getty Images*

Captive cheetahs can be picky about mates.

SANDY HUFFAKER *Getty Images*

CONSERVATION

Tinder for Cheetahs

The scent of urine could help captive big cats find partners

Zoos looking to breed cheetahs in captivity face a serious matchmaking problem. But researchers may have found an unconventional solution: letting feline bachelorettes choose a mate based on the scent of his pee.

New research shows that female cheetahs can detect the genetic relatedness of a potential mate from the smell of his urine alone—and prefer that of more distantly related males. The finding could improve captive-breeding programs and help conserve the speedy cats. "There's so much information that passes through urine. It makes sense that it's a conduit for [the cheetahs] to be able to make a choice on what would be a good mate," says Regina Mossotti, director of animal care and conservation at the Endangered Wolf Center in Eureka, Mo., and lead author of the cheetah study, which was published in the July/August issue of *Zoo Biology.*

Mossotti says zoos hoping to breed cheetahs generally attempt to arrange liaisons with animals at other facilities in an effort to avoid inbreeding—which can result in less healthy offspring. Zoos use a matchmaking system based primarily on genetic similarity, but their calculations do not always result in a mating success.

In the wild, female cheetahs wander far and wide, apparently staking out potential mates by sniffing the scent markings males leave around their territories. So the researchers wanted to test the idea of using urine to introduce possible partners to one another in captivity. Mossotti and her team drove around the U.S. collecting bottles of cheetah pee at various zoos. The researchers then exposed 12 female cheetahs to samples from 17 male "urine donors" of varying genetic relatedness and assessed the big cats' responses to the specimens. They found that females always spent more time in the vicinity of the pee from felines less closely related to them.

Paul Funston, a senior program director at the global wild cat conservation organization Panthera, who was not involved in the research, says it is useful and has a good experimental design—but he questions the utility of zoo breeding programs for these animals. "There's not a lot of evidence that captive cheetahs can be successfully rewilded," he says, but he adds that there may be a better argument for the captive breeding of some particularly endangered subspecies.

The next phase in the research would be to see if this pee test translates to greater mating success. Although doing so may take some work, Mossotti says the team's research is already changing the way zoos think about managing their captive populations. —*Joshua Rapp Learn*

ADVANCES

HEALTH

Postpartum Relief

A new drug could treat a common form of depression after childbirth

Postpartum depression afflicts 10 to 20 percent of the nearly four million women who give birth in the U.S. every year. The condition can interfere with normal bonding between mothers and infants and jeopardize children's development through adolescence. There is no specific treatment, but a promising new drug may change that.

"There is a real need to identify [depressed] women and treat them—and treat them quickly," says Samantha Meltzer-Brody, director of the Perinatal Psychiatry Program at the University of North Carolina Center for Women's Mood Disorders. She conducted recent trials of the drug, which targets hormonal changes in new mothers.

Many women who suffer from postpartum depression receive standard antidepressants, including selective serotonin reuptake inhibitors such as Prozac. It is unclear how well these drugs work, however, because the neurotransmitter serotonin may play only a secondary role in the condition or may not be involved at all. Instead researchers suspect a different biological process may be the culprit.

Pregnancy causes a dramatic rise in the reproductive hormones estrogen and progesterone. It also produces a spike in brain levels of a steroid called allopregnanolone, which normally activates receptors for GABA—a neurochemical that signals brain cells to stop firing. GABA receptors go dormant during pregnancy to avoid overactivation by allopregnanolone; otherwise a pregnant woman would become virtually anesthetized. Immediately following birth, estrogen, progesterone and allopregnanolone drop back to normal levels, after which GABA receptor levels rebound quickly. But in some new mothers, this rebound takes longer, which may result in postpartum depression.

The new drug, developed by Sage Therapeutics, works by elevating allopregnanolone. Doing so activates GABA receptors and keeps the neurochemical at a healthy level. In one of Meltzer-Brody's studies, a phase II clinical trial of 21 severely depressed postpartum women, 70 percent of those who received the drug went into remission. Most important, the effect occurred immediately after it was administered, and benefits persisted for 30 days. Sage Therapeutics has since conducted two phase III trials with a combined 226 postpartum women, and preliminary reports are promising. The drug, called brexanolone, is now under review by the U.S. Food and Drug Administration.

Not everyone is convinced that a single hormonal pathway is responsible, however. Joseph Lonstein, a professor of psychology at Michigan State University, who was not involved in the research, says, "I very much doubt this is the only system that's atypical in women [who] might suffer from postpartum depression or anxiety, but I think it's a completely reasonable one."

—Dana G. Smith

GETTY IMAGES

Claudia Wallis is an award-winning science journalist whose work has appeared in the *New York Times, Time, Fortune* and the *New Republic.* She was science editor at *Time* and managing editor of *Scientific American Mind.*

Coming Down from Opioids

The search is on for safe ways to taper the drugs for people in chronic pain

By Claudia Wallis

Shelley Latin's odyssey with chronic pain and opioids began innocuously enough in June 2011, when she awoke with a stomachache. It took a year for the cause to be correctly diagnosed—a bacterial infection in her gut—and arrested with antibiotics, but by then the pain had taken on a life of its own, no longer linked to the infection. "I couldn't drive, or walk, or sit. I could only lie in bed on my back," she recalls.

Over the next five years Latin, a legal aid lawyer in Oregon, found herself taking ever higher, doctor-prescribed doses of hydrocodone to manage her misery. It was disastrous. She could not focus, she felt crushing fatigue and, inexplicably, she says, "I cried constantly." Worse, her entire abdomen became so hypersensitive that just wearing clothes was painful. This was likely caused in part by a paradoxical side effect of the painkillers known as opioid-induced hyperalgesia.

By last year, Latin had had enough. She enrolled for a week at Stanford University's Comprehensive Interdisciplinary Pain Program, where she worked with doctors to taper her meds, occupational and physical therapists to get moving again, and psychologists to work on her pain-related anxiety and catastrophizing. Now Latin is off opioids and handles her pain with meditation, exercise, psychological counseling and nonopioid nerve pain drugs.

Alas, few of the 10 million or so Americans taking opioids long term for chronic pain have access to such a stellar program. Around the country, state and federal authorities and insurance companies are cracking down on opioid prescriptions in the wake of a 345 percent spike in opioid-related deaths between 2001 and 2016. In some states, legislatures have restricted what doctors can readily prescribe. As a result, many patients are being forced to reduce their drug use without the support to do it safely and effectively. "If somebody is on opioids at high doses for many years, it takes time and work to help them come down from those doses. How any politician thinks they know the answer to this in a one-size-fits-all solution beats me," says opioid researcher Erin Krebs of the Minneapolis Veterans Affairs Health Care System.

In fact, there's very little research on how best to taper opioids for chronic pain patients. For example, although studies show that drugs such as buprenorphine can help addicts recover, little is known about their value in the context of chronic pain. Last year Krebs and her colleagues published a review paper that examined 67 studies on tapering opioids for pain patients and found only three to be of high quality and 13 to be "fair." The good news, Krebs says, "was that as you reduce dosages, most people do better" in terms of pain and quality of life. The challenging news is that the better studies emphasized multidisciplinary care and very close patient follow-up—labor-intensive methods that are not widely available in the U.S. and rarely covered by insurance.

One thing seems clear from research and clinical experience: reckless restriction is not the right response to reckless prescribing. "Forced tapers can destabilize patients," says Stefan Kertesz, an addiction expert at the University of Alabama at Birmingham School of Medicine. Worried clinicians such as Kertesz report growing anecdotal evidence of patient distress and even suicide.

The brightest rays of light in this dark picture come from a burst of new research. In May a team led by Stanford pain psychologist Beth Darnall published the results of a pilot study with 68 chronic pain patients. In four months, the 51 participants who completed the study cut their opioid dosages nearly in half without increased pain. There were no fancy clinics, just an attentive community doctor and a self-help guide written by Darnall. A key element was very slow dose reduction during the first month. "It allows patients to relax into the process and gain a sense of trust with their doctor and with themselves that they can do this," Darnall says. She is now recruiting 1,300 patients for a multicenter study of this method that will also assess the value of adding behavioral support such as cognitive-behavioral therapy.

Other big studies are also getting under way. One headed by Krebs will compare a pharmacist-led program to modify drug regimens with one in which a medical and mental health team helps patients decrease opioid use in the context of setting personal goals. Given the high level of fear that most patients feel about making changes, it's a safe bet that any successful program will be long on patience and compassion. SA

Illustration by Celia Krampien

David Pogue is the anchor columnist for Yahoo Tech and host of several *NOVA* miniseries on PBS.

5G Is Just around the Corner

It will make 4G phones seem positively quaint

By David Pogue

You're probably used to the periodic upgrades in our cell-phone networks. There was 2G, which came along in 1991, replaced with 3G in 2001, followed by 4G in 2009. Now we're hearing about the coming of 5G.

But 5G is a much bigger leap than what's come before. Qualcomm's Web site, in fact, calls it "as transformative as the automobile and electricity." (One of the world's leading makers of phone-networking chips, Qualcomm was a key player in the development of the 5G standard—and stands to profit handsomely from its success.)

Of course, 5G is much faster than 4G—in the real world, a 5G phone in a 5G city will enjoy Internet speeds between nine and 20 times as fast. The latency of 5G (the delay *before* those fast data begin pouring in) is one tenth as long.

The arrival of 5G also means enormous leaps forward in capacity—so much that every cell-phone plan will offer cheap, truly unlimited Internet access. "The consequences of that are immense," says Sherif Hanna, Qualcomm's director of 5G marketing.

For example, apps will no longer degrade your video or postpone downloading when you're out of Wi-Fi range. In fact, you'll probably *prefer* to do your downloads when you're on cellular because 5G will be much faster than whatever service you've got at home or work. Furthermore, our phones can become radically more powerful. Today the processors in our devices are limited by heat and battery capacity. But imagine, Hanna says, if your phone is tied, by a 5G connection, to a much beefier computer online. "It's happening remotely, but because it's such a high-speed connection, it will feel as though the additional processor is inside your device, in your hand," he says.

Another big change: 5G is not just for phones. It reflects the new world of Internet-connected gadgets, industrial machines, farming equipment and even cars. For example, the 5G protocol allows some transmissions to cut in front of others. In, say, 2023 when two self-driving cars need to communicate to avoid a collision, their data will get priority over your stream of *Star Wars: Episode XXV.*

Not everyone is thrilled by the 5G development. The new standard gets its speed partly by using existing transmission frequencies more efficiently and partly by harnessing the millimeter-wave spectrum. That's a big, juicy swath of radio frequencies that are currently underused—because millimeter wave is "really hard to use—very finicky, very tricky," Hanna says.

These frequencies are much higher than anything we've used for cellular. (Your Wi-Fi network uses the 2.4- or 5.8-gigahertz bands. Millimeter wave is 24 gigahertz and up.) Which means they can offer unbelievable speed—but at the expense of range. Millimeter-wave cellular towers have to be about 500 feet apart. Cell carriers not only will have to upgrade all their cell transceivers (called small cells) but will install a lot more of them as well.

That's why the millimeter-wave flavor of 5G—the superfast coverage—will be available only in densely populated cities such as New York and San Francisco. In suburban and rural areas, 5G will bring a speedup of "only" nine times faster.

The need to install more small cells means more rectangular boxes on lampposts, more wires on utility poles and more industrial-looking ugliness in places where local residents don't always want it. Lawsuits, fines and battles between towns and cell carriers are already under way.

But 5G is a train that can't be stopped. The big cell carriers will be turning on 5G in a handful of cities by the end of 2018, and the first 5G-enabled smartphones are expected to go on sale in early 2019. "I don't think most people realize [that] initially 5G was targeted for 2020, and now we're talking about late 2018," Hanna says. "We're working around the clock. Weekends, nights—it's really pretty brutal right now, to be honest."

Here's to all those engineers and their millimeter waves. Someday we'll tell our grandkids about the days when YouTube videos paused annoyingly, people paid for data by the gigabyte and the only way cars could communicate was by honking. SA

SCIENTIFIC AMERICAN ONLINE
READ MORE ABOUT THE IMPLICATIONS OF 5G:
scientificamerican.com/oct2018/pogue

Illustration by Jay Bendt

VERTEX SCIENTIST HONORED FOR 20 YEARS IN THE FIGHT AGAINST CYSTIC FIBROSIS

A conversation with **PAUL NEGULESCU,** Vertex Pharmaceuticals, Senior Vice President and Site Head, San Diego Research

Cystic fibrosis (CF) was once considered untreatable. But over 20 years, Paul Negulescu and a team of scientists at Vertex in San Diego have taken steps to unravel and help treat the disease, in which a genetic defect causes a build-up of mucus in the lungs and digestive system. Those milestones led to Negulescu receiving the 2018 Warren Alpert Foundation Prize this month. He discusses his ongoing journey toward a CF cure.

What is the significance of your being honored with this award?
This Alpert Prize is an example and reminder of what we, as a scientific and medical community, are supposed to do. We are supposed to help people by understanding the cause of diseases and developing therapies that effectively treat or cure them. It's a tremendous feeling to be recognized for contributing to improvements in human health. It's why most of us go into this type of research. This was not an easy or rapid path, so it's wonderful that the work done by so many people for so many years is being recognized. It's a great feeling to acknowledge that our team has stuck together for so long to work on such a difficult challenge. But there's still more that we can do.

Isn't 20 years an unusually long time for a drug discovery project to come to fruition?
Most of the time projects don't get that long to incubate and to deliver. There's a story here about being persistent as long as the science is moving forward. Vertex really supported that process.

Describe Vertex's commitment to CF research.
Our motto is: We are all in for CF. We continue to do research at the same level or higher than five or ten years ago when these compounds were in the early stages. We're continuing to try and come up with better compounds.

What were the signposts that encouraged you?
First, we developed an assay that we thought could be used to test and screen for compounds that might rescue the function of CFTR, the protein compromised by the genetic defect underlying the disease. Then we screened that assay over a million compounds and we got a few hits, which we verified. Then we optimized the compounds to make them suitable as drugs. Then we realized that we probably wouldn't succeed with just one compound.

How did you become interested in CF?
I first learned about CF while doing graduate work in epithelial biology at the University of California, Berkeley. I was studying the role of CFTR in the stomach. Years later, when I was at a biotechnology start-up called Aurora Biosciences, we were approached by the CF Foundation to develop assays and screen compounds that might rescue the function of CFTR. Vertex then bought

IT'S GREAT TO BE TOLD YOU ARE MAKING THINGS BETTER FOR PATIENTS. WE ARE ALL IN FOR CF.

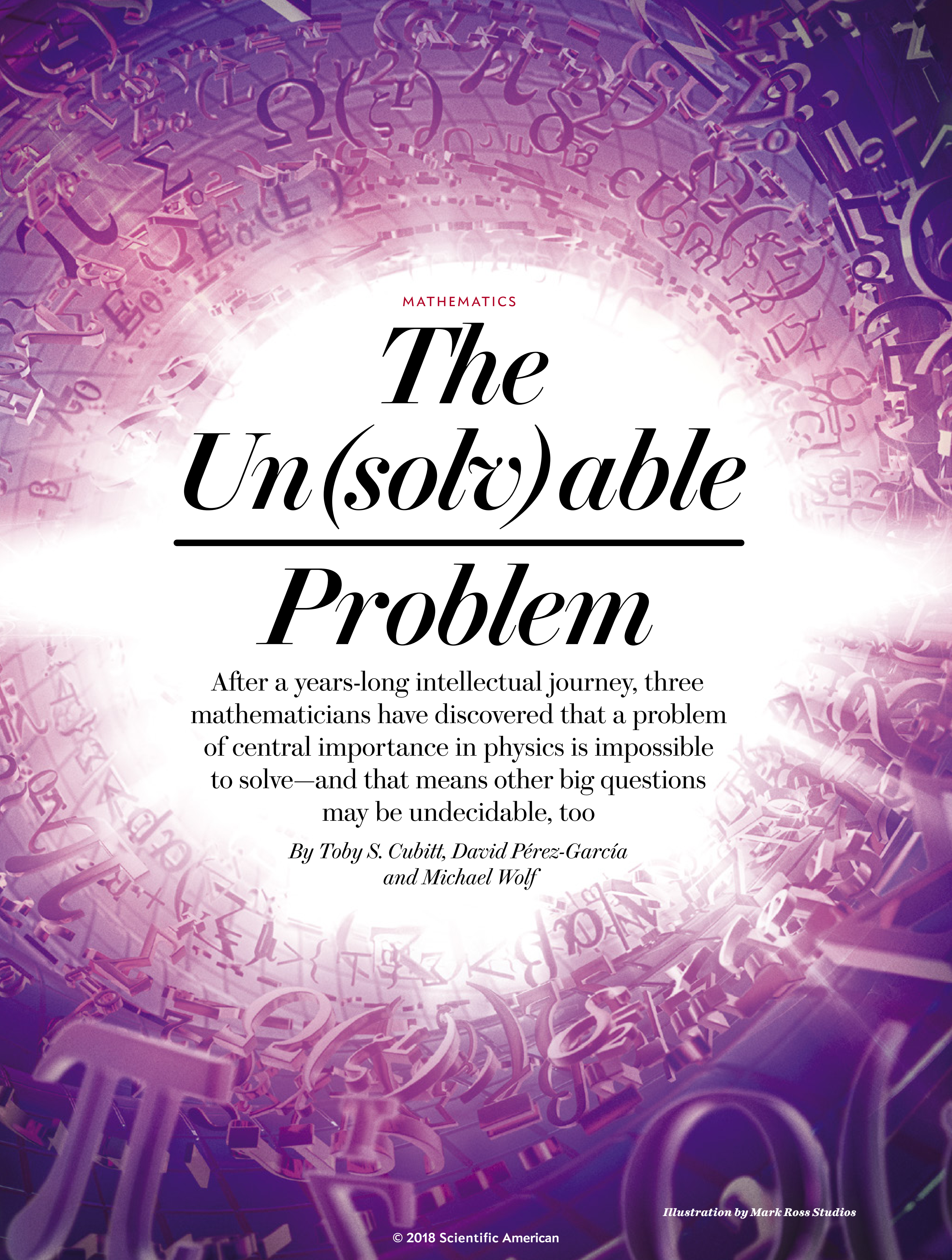
Aurora in 2001 and continued the project. So, it was a case of having the relevant training and then being at the right place at the right time.

Describe the progress made in CF research since you started working on this disease.
In 1989 when the CF gene was identified, the hope was that gene therapy would be the next step. But gene therapy hit some setbacks in the 1990s, so the field tried to focus on symptomatic therapy, like antibiotics. At Vertex, we decided to go after the underlying problems.

Tell me about Vertex's CF pipeline.
We have three approved CFTR modulators on the market. One is a single drug that helps about 10 percent of people with the disease. We also have two approved two-drug combination therapies that cover about 50 percent of those with the disease. We now have two triple drug combinations in clinical research trials that we hope will raise the proportion of treatable CF cases to about 90 percent.

What is the future of CF treatment?
We are moving into the area of genetic-based therapies in terms of thinking about a cure. We have a research collaboration on gene editing for CF. There are better tools available than we had 15 years ago. It's reinvigorating the field.

What's your relationship with the CF community?
The patients have been with us since day one — long before we had any compounds. We'd do fund-raising walks with them. We met some of them as babies or young children and now they are grown up, going to college, and getting treatment. It's great to be told you are making things better for them.



MATHEMATICS

The Un(solv)able Problem

After a years-long intellectual journey, three mathematicians have discovered that a problem of central importance in physics is impossible to solve—and that means other big questions may be undecidable, too

By Toby S. Cubitt, David Pérez-García and Michael Wolf

Illustration by Mark Ross Studios

Toby S. Cubitt is a Royal Society University Research Fellow and reader in quantum information at University College London. After a Ph.D. in physics, postdoctoral positions in mathematics and a faculty position in computer science, he now works on quantum problems that straddle these areas.

David Pérez-García is a professor of mathematics at Complutense University of Madrid and a faculty member at the Institute of Mathematical Sciences in Madrid. He works on mathematical problems in quantum physics.

Michael Wolf is a professor of mathematical physics in the department of mathematics at the Technical University of Munich. His research focuses on the mathematical and conceptual foundations of quantum theory.

THE THREE OF US WERE SITTING TOGETHER IN A CAFÉ IN SEEFELD, A SMALL TOWN DEEP IN THE Austrian Alps. It was the summer of 2012, and we were stuck. Not stuck in the café—the sun was shining, the snow on the Alps was glistening, and the beautiful surroundings were sorely tempting us to abandon the mathematical problem we were stuck on and head outdoors. We were trying to explore the connections between 20th-century mathematical results by Kurt Gödel and Alan Turing and quantum physics. That, at least, was the dream. A dream that had begun back in 2010, during a semester-long program on quantum information at the Mittag-Leffler Institute near Stockholm.

Some of the questions we were looking into had been explored before by others, but to us this line of research was entirely new, so we were starting with something simple. Just then, we were trying to prove a small and not very significant result to get a feel for things. For months now, we had a proof (of sorts) of this result. But to make the proof work, we had to set up the problem in an artificial and unsatisfying way. It felt like changing the question to suit the answer, and we were not very happy with it. Picking the problem up again during the break after the first session of talks at the workshop in Seefeld that had brought us together in 2012, we still could not see any way around our problems. Half-jokingly, one of us (Michael Wolf) asked, "Why don't we prove the undecidability of something people really care about, like the spectral gap?"

At the time, we were interested in whether certain problems in physics are "decidable" or "undecidable"—that is, can they ever be solved? We had gotten stuck trying to probe the decidability of a much more minor question, one few people care about. The "spectral gap" problem Michael was proposing that we tackle (which we will explain later) was one of central importance to physics. We did not know at the time whether this problem was or was not decidable (although we had a hunch it was not) or whether we would be able to prove it either way. But if we could, the results would be of real relevance to physics, not to mention a substantial mathematical achievement. Michael's ambitious suggestion, tossed off almost as a jest, launched us on a grand adventure. Three years and 146 pages of mathematics later, our proof of the undecidability of the spectral gap was published in *Nature*.

To understand what this means, we need to go back to the beginning of the 20th century and trace some of the threads that gave rise to modern physics, mathematics and computer science. These disparate ideas all lead back to German mathematician David Hilbert, often regarded as the greatest figure of the past 100 years in the field. (Of course, no one outside of mathematics has heard of him. The discipline is not a good

IN BRIEF

Kurt Gödel famously discovered in the 1930s that some statements are impossible to prove true or false—they will always be "undecidable."

Mathematicians recently set out to discover whether a certain fundamental problem in quantum physics—the so-called spectral gap question—falls into this category. The spectral gap refers to the energy difference between the lowest energy state a material can occupy and the next state up.

After three years of blackboard brainstorming, midnight calculating and much theorizing over coffee, the mathematicians produced a 146-page proof that the spectral gap problem is, in fact, undecidable. The result raises the possibility that other important questions may likewise be unanswerable.

route to fame and celebrity, although it has its own rewards.)

THE MATHEMATICS OF QUANTUM MECHANICS

HILBERT'S INFLUENCE on mathematics was immense. Early on, he developed a branch of mathematics called functional analysis—in particular, an area known as spectral theory, which would end up being key to the question within our proof. Hilbert was interested in this area for purely abstract reasons. But as so often happens, his mathematics turned out to be exactly what was necessary to understand a question that was perplexing physicists at the time.

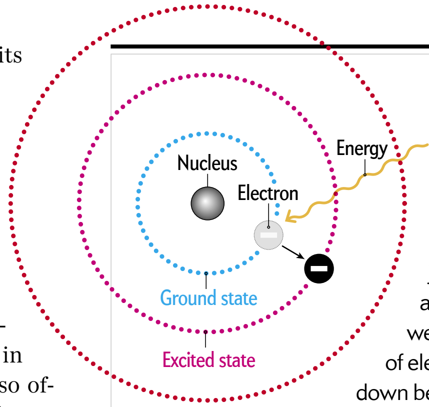
If you heat a substance up, it begins to glow as the atoms in it emit light (hence the phrase "red hot"). The yellow-orange light from sodium street lamps is a good example: sodium atoms predominantly emit light at a wavelength of 590 nanometers, in the yellow part of the visible spectrum. Atoms absorb or release light when electrons within them "jump" between energy levels, and the precise frequency of that light depends on the energy gap between the levels. The frequencies of light emitted by heated materials thus give us a "map" of the gaps between the atom's different energy levels. Explaining these atomic emissions was one of the problems physicists were wrestling with in the first half of the 20th century. The question led directly to the development of quantum mechanics, and the mathematics of Hilbert's spectral theory played a prime role.

One of these gaps between quantum energy levels is especially important. The lowest possible energy level of a material is called its ground state. This is the level it will sit in when it has no heat. To get a material into its ground state, scientists must cool it down to extremely low temperatures in a laboratory. Then, if the material is to do anything other than sit in its ground state, something must excite it to a higher energy. The easiest way is for it to absorb the smallest amount of energy it can, just enough to take it to the next energy level above the ground state—the first excited state. The energy gap between the ground state and this first excited state is so critical that it is often just called the spectral gap.

In some materials, there is a large gap between the ground state and the first excited state. In other materials, the energy levels extend all the way down to the ground state without any gaps at all. Whether a material is "gapped" or "gapless" has profound consequences for its behavior at low temperatures. It plays a particularly significant role in quantum phase transitions.

A phase transition happens when a material undergoes a sudden and dramatic change in its properties. We are all very familiar with some phase transitions—such as water transforming from its solid form of ice into its liquid form when heated up. But there are more exotic quantum phase transitions that happen even when the temperature is kept extremely low. For example, changing the magnetic field around a material or the pressure it is subjected to can cause an insulator to become a superconductor or cause a solid to become a superfluid.

How can a material go through a phase transition at a temperature of absolute zero (−273.15 degrees Celsius), at which there is no heat at all to provide energy? It comes down to the spectral gap. When the spectral gap disappears—when a material is gapless—the energy needed to reach an excited state becomes zero. The tiniest amount of energy will be enough to push the material through a phase transition. In fact, thanks to

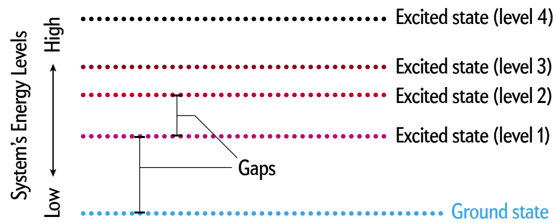


The Spectral Gap

The authors' mathematical proof took on the question of the "spectral gap"—the jump in energy between the ground state and first excited state of a material. When we think of energy states, we tend to think of electrons in atoms, which can jump up and down between energy levels. Whereas in atoms there is always a gap between such levels, in larger materials made of many atoms, there is sometimes no distance between the ground state and the first excited state: even the smallest possible amount of energy will be enough to push the material up an energy level. Such materials are called "gapless." The authors proved that it will never be possible to determine whether all materials are gapped or gapless.

Gapped System

There are discrete gaps between each energy level, and the material must reach a certain energy to make the leap to the next level.



Gapless System

No expanse separates the ground state and first excited state, and the material may become excited with just the tiniest input of energy.

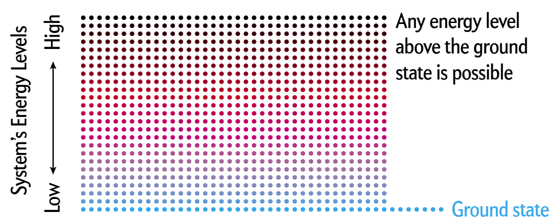
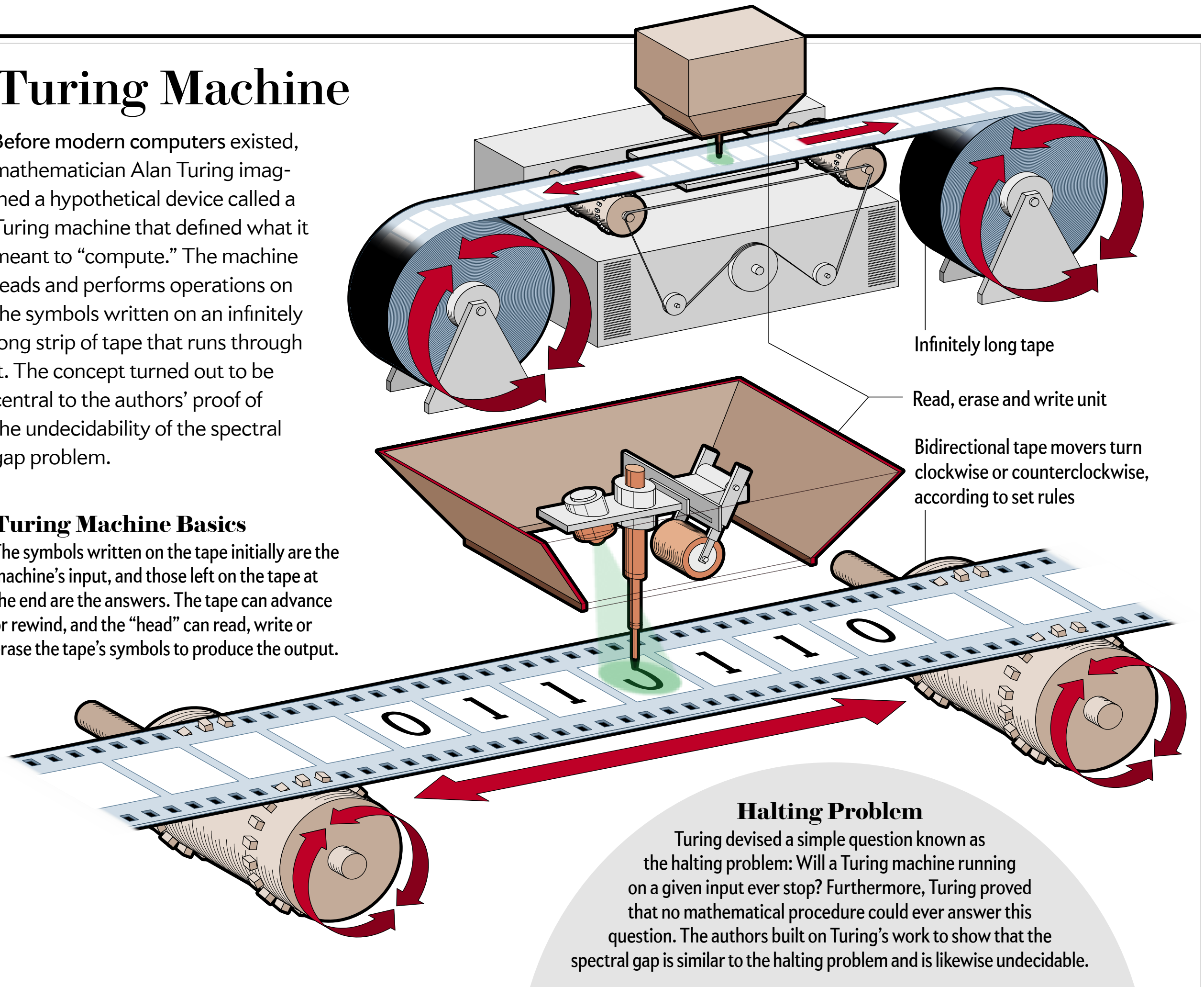


Illustration by Jen Christiansen

Turing Machine

Before modern computers existed, mathematician Alan Turing imagined a hypothetical device called a Turing machine that defined what it meant to "compute." The machine reads and performs operations on the symbols written on an infinitely long strip of tape that runs through it. The concept turned out to be central to the authors' proof of the undecidability of the spectral gap problem.



the weird quantum effects that dominate physics at these very low temperatures, the material can temporarily "borrow" this energy from nowhere, go through a phase transition and "give" the energy back. Therefore, to understand quantum phase transitions and quantum phases, we need to determine when materials are gapped and when they are gapless.

Because this spectral gap problem is so fundamental to understanding quantum phases of matter, it crops up all over the place in theoretical physics. Many famous and long-standing open problems in condensed matter physics boil down to solving this problem for a specific material. A closely related question even crops up in particle physics: there is very good evidence that the fundamental equations describing quarks and their interactions have a "mass gap." Experimental data from particle colliders such as the Large Hadron Collider near Geneva support this notion, as do massive number-crunching results from supercomputers. But proving the idea rigorously from the theory seems to be extremely difficult. So difficult, in fact, that this problem, called the Yang-Mills mass gap problem, has been named one of seven Millennium Prize problems by the Clay Mathematics Institute, and anyone who solves it is entitled to a $1-million prize. All these problems are particular cases of the general spectral gap question. We have bad news for anyone trying to solve them, though. Our proof shows that the general problem is even trickier than we thought. The reason comes down to a question called the *Entscheidungsproblem*.

UNANSWERABLE QUESTIONS

BY THE 1920S Hilbert had become concerned with putting the foundations of mathematics on a firm, rigorous footing—an endeavor that became known as Hilbert's program. He believed that whatever mathematical conjecture one might make, it will in principle be possible to prove either that it is true or that it is false. (It had better not be possible to prove that it is both, or something has gone very wrong with mathematics!) This idea might seem obvious, but mathematics is about establishing concepts with absolute certainty. Hilbert wanted a rigorous proof.

In 1928 he formulated the *Entscheidungsproblem*. Although it sounds like the German sound for a sneeze, in English it translates to "the decision problem." It asks whether there is a procedure, or "algorithm," that can decide whether mathematical statements are true or false.

For example, the statement "Multiplying any whole number by 2 gives an even number" can easily be proved true, using basic logic and arithmetic. Other statements are less clear. What about the following example? "If you take any whole number,

Illustration by Ben Gilliland

and repeatedly multiply it by 3, and add 1 if it's odd or divide it by 2 if it's even, you always eventually reach the number 1." (Have a think about it.)

Unfortunately for Hilbert, his hopes were to be dashed. In 1931 Gödel published some remarkable results now known as his incompleteness theorems. Gödel showed that there are perfectly reasonable mathematical statements about whole numbers that can be neither proved nor disproved. In a sense, these statements are beyond the reach of logic and arithmetic. And he proved this assertion. If that is hard to wrap your head around, you are in good company. Gödel's incompleteness theorems shook the foundations of mathematics to the core.

Here is a flavor of Gödel's idea: If someone tells you, "This sentence is a lie," is that person telling the truth or lying? If he or she is telling the truth, then the statement must indeed be a lie. But if he or she is lying, then it is true. This quandary is known as the liar paradox. Even though it appears to be a perfectly reasonable English sentence, there is no way to determine whether it is true or false. What Gödel managed to do was to construct a rigorous mathematical version of the liar paradox using only basic arithmetic.

The next major player in the story of the *Entscheidungsproblem* is Alan Turing, the English computer scientist. Turing is most famous among the general public for his role in breaking the German Enigma code during World War II. But among scientists, he is best known for his 1937 paper "On Computable Numbers, with an Application to the *Entscheidungsproblem*." Strongly influenced by Gödel's result, the young Turing had given a negative answer to Hilbert's *Entscheidungsproblem* by proving that no general algorithm to decide whether mathematical statements are true or false can exist. (American mathematician Alonzo Church also independently proved this just before Turing. But Turing's proof was ultimately more significant. Often in mathematics, the proof of a result turns out to be more important than the result itself.)

To solve the *Entscheidungsproblem,* Turing had to pin down precisely what it meant to "compute" something. Nowadays we think of computers as electronic devices that sit on our desk, on our lap or even in our pocket. But computers as we know them did not exist in 1936. In fact, "computer" originally meant a person who carried out calculations with pen and paper. Nevertheless, computing with pen and paper as you did in high school is mathematically no different to computing with a modern desktop computer—just much slower and far more prone to mistakes.

Turing came up with an idealized, imaginary computer called a Turing machine. This very simple imaginary machine does not look like a modern computer, but it can compute everything that the most powerful modern computer can. In fact, any question that can ever be computed (even on quantum computers or computers from the 31st century that have yet to be invented) could also be computed on a Turing machine. It would just take the Turing machine much longer.

A Turing machine has an infinitely long ribbon of tape and a "head" that can read and write one symbol at a time on the tape, then move one step to the right or left along it. The input to the computation is whatever symbols are originally written on the tape, and the output is whatever is left written on it when the Turing machine finally stops running (halts). The invention of the Turing machine was more important even than the solution to the *Entscheidungsproblem*. By giving a precise, mathematically rigorous formulation of what it meant to make a computation, Turing founded the modern field of computer science.

Having constructed his imaginary mathematical model of a computer, Turing then went on to prove that there is a simple question about Turing machines that no mathematical procedure can ever decide: Will a Turing machine running on a given input ever halt? This question is known as the halting problem. At the time, this result was shocking. Mathematicians have become accustomed to the fact that any conjecture we are working on could be provable, disprovable or undecidable.

WHERE WE COME IN

IN OUR RESULT, we had to tie all these disparate threads back together. We wanted to unite the quantum mechanics of the spectral gap, the computer science of undecidability and Hilbert's spectral theory to prove that—like the halting problem—the spectral gap problem was one of the undecidable ones that Gödel and Turing taught us about.

Chatting in that café in Seefeld in 2012, we had an idea for how we might be able to prove a weaker mathematical result related to the spectral gap. We tossed this idea around, not even scribbling on the back of a napkin, and it seemed like it might work. Then the next session of talks started. And there we left it.

A few months later one of us (Toby Cubitt) visited Michael in Munich, and we did what we had not done in Seefeld: jotted some equations down on a scrap of paper and convinced ourselves the idea worked. In the following weeks, we completed the argument and wrote it up properly in a private four-page note. (Nothing in mathematics is truly proved until you write it down—or, better still, type it up and show it to a colleague for scrutiny.) Conceptually this was a major advance. Before now, the idea of proving the undecidability of the spectral gap was more of a joke than a serious prospect. Now we had the first glimmerings that it might actually be possible. But there was still a very long way to go. We could not extend our initial idea to prove the undecidability of the spectral gap problem itself.

BURNING THE MIDNIGHT COFFEE

WE ATTEMPTED to make the next leap by linking the spectral gap problem to quantum computing. In 1985 Nobel Prize–winning physicist Richard Feynman published one of the papers that launched the idea of quantum computers. In that paper, Feynman showed how to relate ground states of quantum systems to computation. Computation is a dynamic process: you supply the computer with input, and it goes through several steps to compute a result and outputs the answer. But ground states of quantum systems are completely static: the ground state is just the configuration a material sits in at zero temperature, doing nothing at all. So how can it make a computation?

The answer comes through one of the defining features of quantum mechanics: superposition, which is the ability of objects to occupy many states simultaneously, as, for instance, Erwin Schrödinger's famous quantum cat can be alive and dead at the same time. Feynman proposed constructing a quantum state that is in a superposition of the various steps in a computation—initial input, every intermediate step of the computation and final output—all at once. Alexei Kitaev of the California Institute of Technology later developed this idea substantially by constructing an imaginary quantum material whose ground state looks exactly like this.

If we used Kitaev's construction to put the entire history of a Turing machine into the material's ground state in superposition, could we transform the halting problem into the spectral gap problem? In other words, could we show that any method for solving the spectral gap problem would also solve the halting problem? Because Turing had already shown that the halting problem was undecidable, this would prove that the spectral gap problem must also be undecidable.

Encoding the halting problem in a quantum state was not a new idea. Seth Lloyd, now at the Massachusetts Institute of Technology, had proposed this almost two decades earlier to show the undecidability of another quantum question. Daniel Gottesman of the Perimeter Institute for Theoretical Physics in Waterloo and Sandy Irani of the University of California, Irvine, had used Kitaev's idea to prove that even single lines of interacting quantum particles can show very complex behavior. In fact, it was Gottesman and Irani's version of Kitaev's construction that we hoped to make use of.

But the spectral gap is a different kind of problem, and we faced some apparently insurmountable mathematical obstacles. The first had to do with supplying the input into the Turing machine. Remember that the undecidability of the halting problem is about whether the Turing machine halts *on a given input*. How could we design our imaginary quantum material in a way that would let us choose the input to the Turing machine to be encoded in the ground state?

When working on that earlier problem (the one we were still stuck on in the café in Seefeld), we had an idea of how to rectify the issue by putting a "twist" in the interactions between the particles and using the angle of this rotation to create an input to the Turing machine. In January 2013 we met at a conference in Beijing and discussed this plan together. But we quickly realized that what we had to prove came very close to contradicting known results about quantum Turing machines. We decided we needed a complete and rigorous proof that our idea worked before we pursued the project further.

At this point, Toby had been part of David Pérez-García's group at Complutense University of Madrid for more than two years. In that same month he moved to the University of Cambridge, but his new apartment there was not yet ready, so his friend and fellow quantum information theorist Ashley Montanaro offered to put him up. For those two months, he set to work producing a rigorous proof of this idea. His friend would find him at the kitchen table in the morning, a row of empty coffee mugs next to him, about to head to bed, having worked through the night figuring out details and typing them up. At the end of those two months, Toby sent around the completed proof.

IN REMEMBRANCE OF TILINGS PAST

THIS 29-PAGE PROOF showed how to overcome one of the obstacles to connecting the ground state of a quantum material to computation with a Turing machine. But there was an even bigger obstacle to that goal: the resulting quantum material was always

Tiling an Infinite Bathroom Floor

To connect the spectral gap problem to the halting problem, the authors considered the classic mathematical question of how to tile an infinitely large floor. Imagine you have a box with a certain selection of tiles, and you want to arrange them so that the colors on the sides of each tile match those next to them. In some cases, this is possible by tiling the floor in either a repeating "periodic" pattern or a fractal-like "aperiodic" pattern.

Periodic Tiles

One version of the classic problem concerns tiles that come in three varieties containing five different colors. In this particular case, it is possible to tile the floor with all sides matching up by creating a rectangle that repeats. On each side of the rectangle, the colors match so that many versions of the same rectangle can be placed next to one another in an infinite pattern.

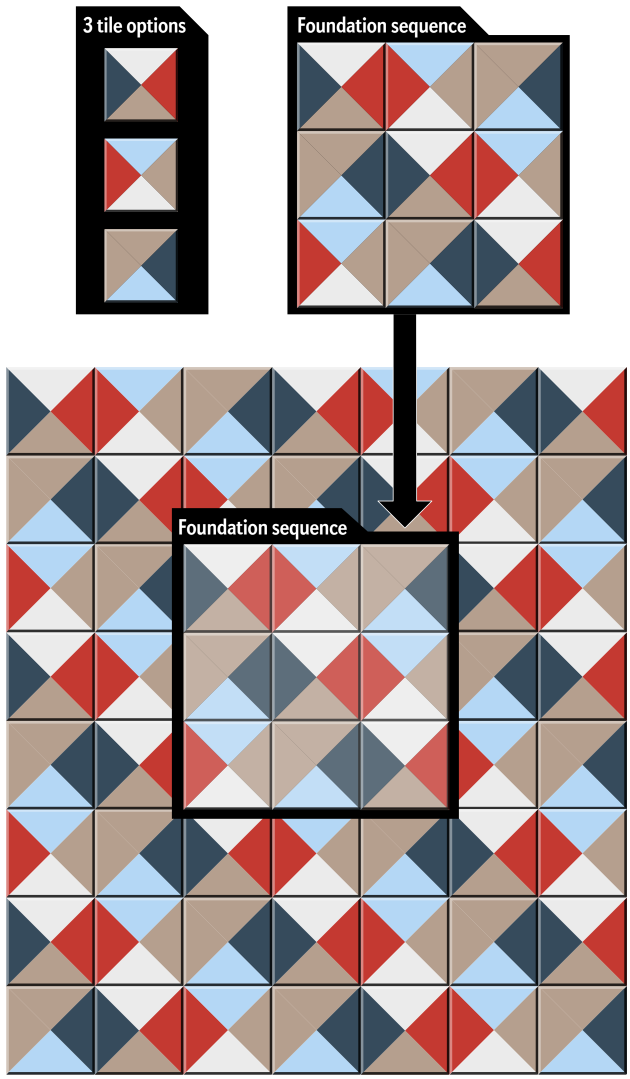
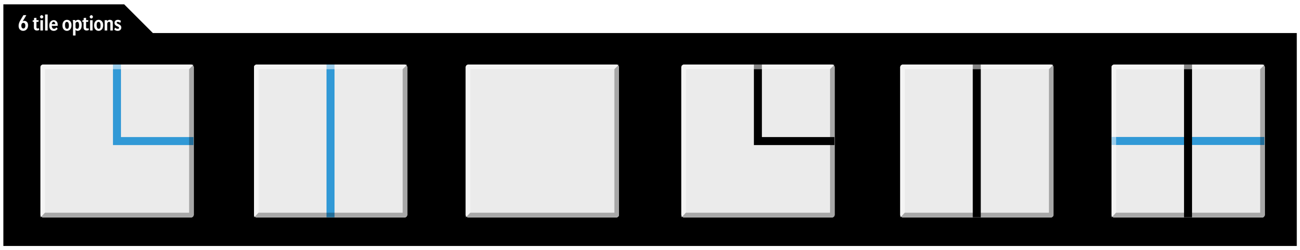
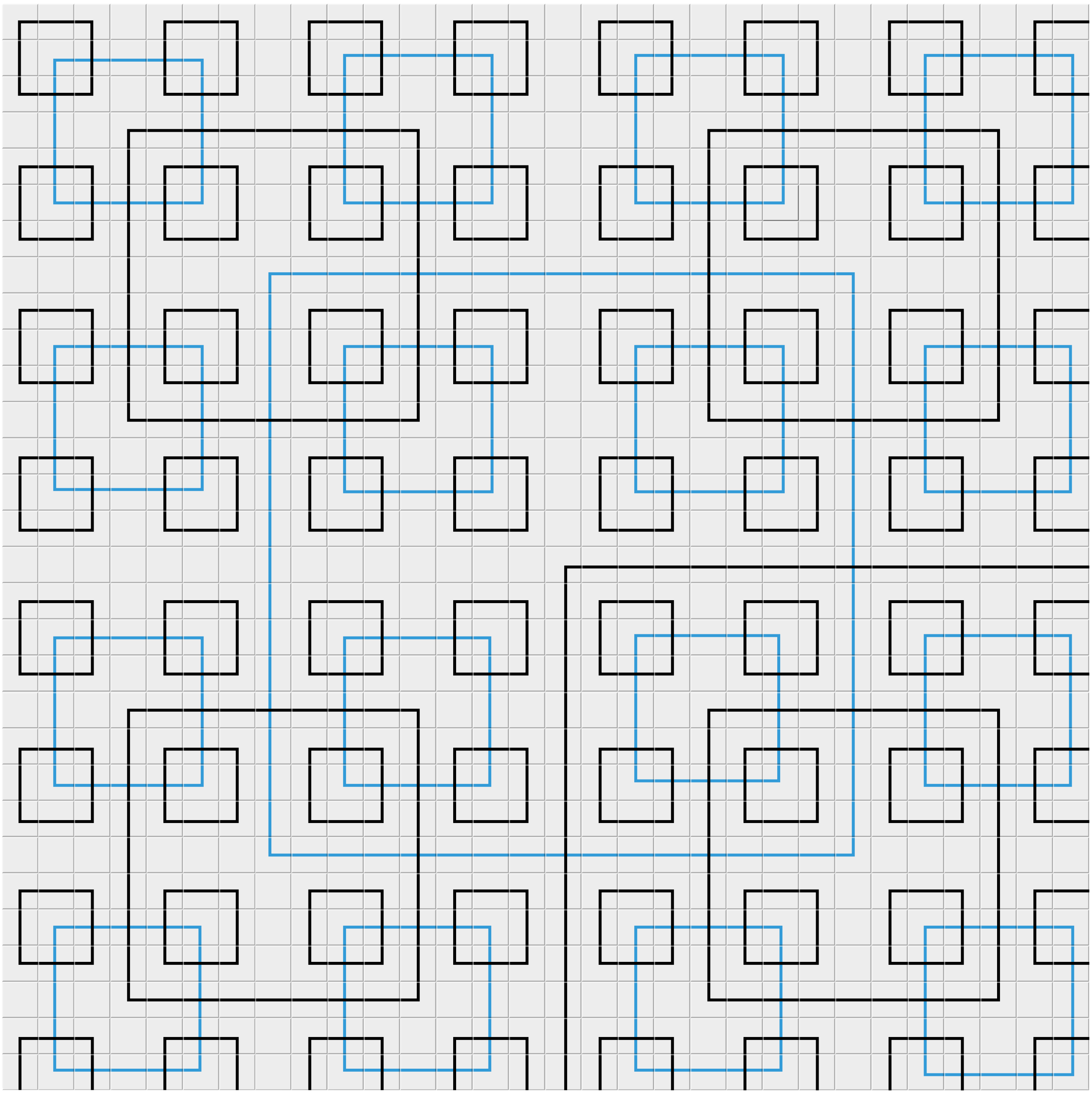


Illustration by Jen Christiansen

Aperiodic Tiles

In their proof, the authors used a particular set of tiles designed by mathematician Rafael Robinson in 1971. Robinson's tiles fit together in an ever expanding sequence that does not quite repeat but instead creates a fractal-like pattern. All rotations of the six tiles shown here are allowed. There are also other ways to fit these pieces together in a periodic pattern, but by adding more markings to these tiles (*not shown*), Robinson designed a set of 56 tiles for which no pattern is possible other than the one shown.





gapless. If it is always gapless, the spectral gap problem for this particular material is very easy to solve: the answer is gapless!

Our first idea from Seefeld, which proved a much weaker result than we wanted, nonetheless managed to get around this obstacle. The key was using "tilings." Imagine you are covering a large bathroom floor with tiles. In fact, imagine it is an infinitely big bathroom. The tiles have a very simple pattern on them: each of the four sides of the tile is a different color. You have various boxes of tiles, each with a different arrangement of colors. Now imagine there is an infinite supply of tiles in each box. You, of course, want to tile the infinite bathroom floor so that the colors on adjacent tiles match. Is this possible?

The answer depends on which boxes of tiles you have available. With some sets of colored tiles, you will be able to tile the infinite bathroom floor. With others, you will not. Before you select which boxes of tiles to buy, you would like to know whether or not they will work. Unfortunately for you, in 1966 mathematician Robert Berger proved that this problem is undecidable.

One easy way to tile the infinite bathroom floor would be to first tile a small rectangle so that colors on opposite sides of it match. You could then cover the entire floor by repeating this rectangular pattern. Because they repeat every few tiles, such patterns are called periodic. The reason the tiling problem is undecidable is that nonperiodic tilings also exist: patterns that cover the infinite floor but never repeat.

Back when we were discussing our first small result, we studied a 1971 simplification of Berger's original proof made by Rafael Robinson of the University of California, Berkeley. Robinson constructed a set of 56 different boxes of tiles that, when used to tile the floor, produce an interlocking pattern of ever larger squares. This fractal pattern looks periodic, but in fact, it never quite repeats itself. We extensively discussed ways of using tiling results to prove the undecidability of quantum properties. But back then, we were not even thinking about the spectral gap. The idea lay dormant.

In April 2013 Toby paid a visit to Charlie Bennett at IBM's Thomas J. Watson Research Center. Among Bennett's many achievements before becoming one of the founding fathers of quantum information theory was his seminal 1970s work on Turing machines. We wanted to quiz him about some technical details of our proof to make sure we were not overlooking something. He said he had not thought about this stuff for 40 years, and it was high time a younger generation took over. (He then went on to very helpfully explain some subtle mathematical details of his 1970s work, which reassured us that our proof was okay.)

Bennett has an immense store of scientific knowledge. Because we had been talking about Turing machines and undecidability, he e-mailed copies of a couple of old papers on undecidability he thought might interest us. One of these was the same 1971 paper by Robinson that we had studied. Now the time was right for the ideas sowed in our earlier discussions to spring to life. Reading Robinson's paper again, we realized it was exactly what we needed to prevent the spectral gap from vanishing.

Our initial idea had been to encode one copy of the Turing machine into the ground state. By carefully designing the interactions between the particles, we could make the ground state energy a bit higher if the Turing machine halted. The spectral gap—the energy jump to the first excited state—would then depend on whether the Turing machine halted or not. There was just one problem with this idea, and it was a big one. As the number of particles increased, the additional contribution to the ground state energy got closer and closer to zero, leading to a material that was always gapless.

But by adapting Berger's tiling construction, we could instead encode *many copies* of exactly the same Turing machine into the ground state. In fact, we could attach one copy to each square in Robinson's tiling pattern. Because these are identical copies of the same Turing machine, if one of them halts, they all halt. The energy contributions from all these copies add up. As the number of particles increases, the number of squares in the tiling pattern gets bigger. Thus, the number of copies of the Turing machine increases, and their energy contribution becomes huge, giving us the possibility of a spectral gap.

EXAMS AND DEADLINES

ONE SIGNIFICANT WEAKNESS remained in the result we had proved. We could not say anything about how *big* the energy gap was when the material was gapped. This uncertainty left our result open to the criticism that the gap could be so small that it might as well not exist. We needed to prove that the gap, when it existed, was actually large. The first solution we found arose by considering materials in three dimensions instead of the planar materials we had been thinking about until then.

When you cannot stop thinking about a mathematical problem, you make progress in the most unexpected places. David worked on the details of this idea in his head while he was supervising an exam. Walking along the rows of tables in the hall, he was totally oblivious to the students working feverishly around him. Once the test was over, he committed this part of the proof to paper.

We now knew that getting a big spectral gap was possible. Could we also get it in two dimensions, or were three necessary? Remember the problem of tiling an infinite bathroom floor. What we needed to show was that for the Robinson tiling, if you got one tile wrong somewhere, but the colors still matched everywhere else, then the pattern formed by the tiles would be disrupted only in a small region centered on that wrong tile. If we could show this "robustness" of the Robinson tiling, it would imply that there was no way of getting a small spectral gap by breaking the tiling only a tiny bit.

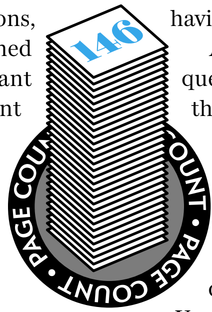
By the late summer of 2013, we felt we had all the ingredients for our proof to work. But there were still some big details to be resolved, such as proving that the tiling robustness could be merged with all the other proof ingredients to give the complete result. The Isaac Newton Institute for Mathematical Science in Cambridge, England, was hosting a special workshop on quantum information for the whole of the autumn semester of 2013. All three of us were invited to attend. It was the perfect opportunity to work together on finishing the project. But David was not able to stay in Cambridge for long. We were determined to complete the proof before he left.

The Isaac Newton Institute has blackboards everywhere—even in the bathrooms! We chose one of the blackboards in a corridor (the closest to the coffee machine) for our discussions. We spent long hours at the blackboard developing the missing ideas, then divided the task of making these ideas mathematically rig-

orous among us. This process always takes far more time and effort than it seems on the blackboard. As the date of David's departure loomed, we worked without interruption all day and most of the night. Just a few hours before he left for home, we finally had a complete proof.

In physics and mathematics, researchers make most results public for the first time by posting a draft paper to the arXiv.org preprint server before submitting it to a journal for peer review. Although we were now fairly confident the entire argument worked and the hardest part was behind us, our proof was not ready to be posted. There were many mathematical details to be filled in. We also wanted to rewrite and tidy up the paper (we hoped to reduce the page count in the process, although in this we would completely fail). Most important, although at least one of us had checked every part of the proof, no one had gone through it all from beginning to end.

In summer 2014 David was on a sabbatical at the Technical University of Munich with Michael. Toby went out to join them. The plan was to spend this time checking and completing the whole proof, line by line. David and Toby were sharing an office. Each morning David would arrive with a new printout of the draft paper, copious notes and questions scribbled in the margins and on interleaved sheets. The three of us would get coffee and then pick up where we had left off the day before, discussing the next section of the proof at the blackboard. In the afternoon, we divided up the work of rewriting the paper and adding the new material and of going through the next section of the proof. Toby was suffering from a slipped disc and could not sit down, so he worked with his laptop propped on top of an upturned garbage bin on top of the desk. David sat opposite, the growing pile of printouts and notes taking up more and more of his desk. On a couple of occasions, we found significant gaps in the proof. These turned out to be surmountable, but bridging them meant adding substantial material to it. The page count continued to grow.



After six weeks, we had checked, completed and improved every single line of the proof. It would take another six months to finish writing everything up. Finally, in February 2015, we uploaded the paper to arXiv.org.

WHAT IT ALL MEANS

ULTIMATELY what do these 146 pages of complicated mathematics tell us?

First, and most important, they give a rigorous mathematical proof that one of the basic questions of quantum physics cannot be solved in general. Note that the "in general" here is critical. Even though the halting problem is undecidable in general, for *particular* inputs to a Turing machine, it is often still possible to say whether it will halt or not. For example, if the first instruction of the input is "halt," the answer is pretty clear. The same goes if the first instruction tells the Turing machine to loop forever. Thus, although undecidability implies that the spectral gap problem cannot be solved for *all* materials, it is entirely possible to solve it for specific materials. In fact, condensed matter physics is littered with such examples. Nevertheless, our result proves rigorously that even a perfect, complete description of the microscopic interactions between a material's particles is not always enough to deduce its macroscopic properties.

You may be asking yourself if this finding has any implications for "real physics." After all, scientists can always try to measure the spectral gap in experiments. Imagine if we could engineer the quantum material from our mathematical proof and produce a piece of it in the lab. Its interactions are so extraordinarily complicated that this task is far, far beyond anything scientists are ever likely to be able to do. But if we could and then took a piece of it and tried to measure its spectral gap, the material could not simply throw up its hands and say, "I can't tell you—it's undecidable." The experiment would have to measure *something*.

The answer to this apparent paradox lies in the fact that, strictly speaking, the terms "gapped" and "gapless" only make mathematical sense when the piece of material is infinitely large. Now, the 10^{23} or so atoms contained in even a very small piece of material represent a very large number indeed. For normal materials, this is close enough to infinity to make no difference. But for the very strange material constructed in our proof, large is not equivalent to infinite. Perhaps with 10^{23} atoms, the material appears in experiments to be gapless. Just to be sure, you take a sample of material twice the size and measure again. Still gapless. Then, late one night, your graduate student comes into the lab and adds just one extra atom. The next morning, when you measure it again, the material has become gapped! Our result proves that the size at which this transition may occur is incomputable (in the same Gödel-Turing sense that you are now familiar with). This story is completely hypothetical for now because we cannot engineer a material this complex. But it shows, backed by a rigorous mathematical proof, that scientists must take special care when extrapolating experimental results to infer the behavior of the same material at larger sizes.

And now we come back to the Yang-Mills problem—the question of whether the equations describing quarks and their interactions have a mass gap. Computer simulations indicate that the answer is yes, but our result suggests that determining for sure may be another matter. Could it be that the computer-simulation evidence for the Yang-Mills mass gap would vanish if we made the simulation just a tiny bit larger? Our result cannot say, but it does open the door to the intriguing possibility that the Yang-Mills problem, and other problems important to physicists, may be undecidable.

And what of that original small and not very significant result we were trying to prove all those years ago in a café in the Austrian Alps? Actually, we are still working on it. SA

MORE TO EXPLORE

Undecidability and Nonperiodicity for Tilings of the Plane. Raphael M. Robinson in *Inventiones Mathematicae,* Vol. 12, No. 3, pages 177–209; September 1971.

Undecidability of the Spectral Gap. Toby S. Cubitt, David Pérez-García and Michael M. Wolf in *Nature,* Vol. 528, pages 207–211; December 10, 2015. Preprint available at https://arxiv.org/abs/1502.04573

FROM OUR ARCHIVES

Ultimate Clocks. W. Wayt Gibbs; September 2002.

scientificamerican.com/magazine/sa

ARTIFICIAL INTELLIGENCE

CLICKS, LIES AND VIDEOTAPE

Artificial intelligence is making it possible for anyone to manipulate audio and video. The biggest threat is that we stop trusting anything at all

By Brooke Borel

IN BRIEF

Rapidly evolving AI technologies allow for the automated creation of fake video and audio. Some experts worry that the spread of disinformation via social media could have profound effects on public discourse and political stability.

Computer scientists are working on AI detection tools to flag fake videos, but they lag behind the ability to create manipulated content. Meanwhile social scientists warn that policing fakes post hoc is not a sufficient solution.

Written fake news was a troubling factor in the 2016 U.S. elections. Research suggests that fake video may be especially effective at stoking fear—an emotion that powers viral content. One concern is that it could erode our trust in all media, including what is real.

Illustration by Taylor Callery

Brooke Borel is a journalist and author of *The Chicago Guide to Fact-Checking*. She recently competed against an AI fact-checker and won by a worrying margin.

THIS PAST APRIL A NEW VIDEO OF BARACK OBAMA SURFACED ON THE INTERNET. AGAINST A backdrop that included both the American and presidential flags, it looked like many of his previous speeches. Wearing a crisp white shirt and dark suit, Obama faced the camera and punctuated his words with outstretched hands: "President Trump is a total and complete dipshit."

Without cracking a smile, he continued. "Now, you see, I would never say these things. At least not in a public address. But someone else would." The view shifted to a split screen, revealing the actor Jordan Peele. Obama hadn't said anything—it was a real recording of an Obama address blended with Peele's impersonation. Side by side, the message continued as Peele, like a digital ventriloquist, put more words in the former president's mouth.

In this era of fake news, the video was a public service announcement produced by BuzzFeed News, showcasing an application of new artificial-intelligence (AI) technology that could do for audio and video what Photoshop has done for digital images: allow for the manipulation of reality.

The results are still fairly unsophisticated. Listen and watch closely, and Obama's voice is a bit nasally. For brief flashes, his mouth—fused with Peele's—floats off-center. But this rapidly evolving technology, which is intended for Hollywood film editors and video game makers, has the imaginations of some national security experts and media scholars running dark. The next generation of these tools may make it possible to create convincing fakes from scratch—not by warping existing footage, as in the Obama address, but by orchestrating scenarios that never happened at all.

The consequences for public knowledge and discourse could be profound. Imagine, for instance, the impact on the upcoming midterm elections if a fake video smeared a politician during a tight race. Or attacked a CEO the night before a public offering. A group could stage a terrorist attack and fool news outlets into covering it, sparking knee-jerk retribution. Even if a viral video is later proved to be fake, will the public still believe it was true anyway? And perhaps most troubling: What if the very idea of pervasive fakes makes us stop believing much of what we see and hear—including the stuff that is real?

Many technologists acknowledge the potential for sweeping misuse of this technology. But while they fixate on "sexy solutions for detection and disclosure, they spend very little time figuring out whether any of that actually has an effect on people's beliefs on the validity of fake video," says Nate Persily, a law professor at Stanford University. Persily studies, among other topics, how the Internet affects democracy, and he is among a growing group of researchers who argue that curbing viral disinformation cannot be done through technical fixes alone. It will require input from psychologists, social scientists and media experts to help tease out how the technology will land in the real world.

"We've got to do this now," Persily says, "because at the moment the technologists—necessarily—drive the discussion" on what may be possible with AI-generated video. Already, our trust in democratic institutions such as government and journalism is ebbing. With social media a dominant distribution channel for information, it is even easier today for fake-news makers to exploit us. And with no cohesive strategy in place to confront an increasingly sophisticated technology, our fragile collective trust is even more at risk.

INNOCUOUS BEGINNINGS

THE PATH TO FAKE VIDEO traces back to the 1960s, when computer-generated imagery was first conceived. In the 1980s these special effects went mainstream, and ever since, movie lovers have watched the technology evolve from science-fiction flicks to Forrest Gump shaking hands with John F. Kennedy in 1994 to the revival of Peter Cushing and Carrie Fisher in *Rogue One*. The goal has always been to "create a digital world where any storytelling could be possible," says Hao Li, an assistant professor of computer science at the University of Southern California and CEO of Pinscreen, an augmented-reality start-up. "How can we create something that appears real, but everything is actually virtual?"

Early on, most graphics came from artists, who used computers to create three-dimensional models and then hand-painted textures and other details—a tedious process that did not scale up. About 20 years ago some computer-vision researchers started thinking of graphics differently: rather than spending time on individual models, why not teach computers to create from data? In 1997 scientists at the Interval Research Corporation in Palo Alto, Calif., developed Video Rewrite, which sliced up existing footage and reconfigured it. The researchers made a clip of JFK

TECHNOLOGY that was originally developed to create virtual scenes in film (*1*) has evolved into a tool that can be used to make fake videos (*2*) to spread disinformation.

FILM STILL FROM *FORREST GUMP*, PARAMOUNT PICTURES, 1994 (*1*); FILM STILL FROM *YOU WON'T BELIEVE WHAT OBAMA SAYS IN THIS VIDEO!* MONKEYPAW PRODUCTIONS AND BUZZFEED, APRIL 17, 2018 (*2*)

saying, "I never met Forrest Gump." Soon after, scientists at the Max Planck Institute for Biological Cybernetics in Tübingen, Germany, taught a computer to pull features from a data set of 200 three-dimensional scans of human faces to make a new face.

The biggest recent jump in the relationship among computer vision, data and automation arguably came in 2012, with advances in a type of AI called deep learning. Unlike the work from the late 1990s, which used static data and never improved, deep learning adapts and gets better. This technique reduces objects, such as a face, to bits of data, says Xiaochang Li, a postdoctoral fellow at the Max Planck Institute for the History of Science in Berlin. "This is the moment where engineers say: we are no longer going to model things," she says. "We are going to model our ignorance of things, and just run the data to understand patterns."

Deep learning uses layers of simple mathematical formulas called neural networks, which get better at a task over time. For example, computer scientists can teach a deep-learning tool to recognize human faces by feeding it hundreds or thousands of photographs and essentially saying, each time, *this is a face* or *this is not a face*. Eventually when the tool encounters a new person, it will recognize patterns that make up human features and say, statistically speaking, *this is also a face*.

Next came the ability to concoct faces that looked like real people, using deep-learning tools known as generative networks. The same logic applies: computer scientists train the networks on hundreds or thousands of images. But this time the network follows the patterns it gleaned from the examples to make a new face. Some companies are now using the same approach with audio. Earlier this year Google unveiled Duplex, an AI assistant based on software called WaveNet, which can make phone calls and sounds like a real person—complete with verbal tics such as uhs and hmms. In the future, a fake video of a politician may not need to rely on impersonations from actors like Peele. In April 2017 Lyrebird, a Canadian start-up, released sample audio that sounded creepily like Obama, Trump and Hillary Clinton.

But generative networks need big data sets for training, and that can require significant human labor. The next step in improving virtual content was to teach the AI to train itself. In 2014 researchers at the University of Montreal did this with a generative adversarial network, or GAN, which puts two neural networks in conversation. The first is a generator, which makes fake images, and the second is a discriminator, which learns to distinguish between real and fake. With little to no human supervision, the networks train one another through competition—the discriminator nudges the generator to make increasingly realistic fakes, while the generator keeps trying to trick the discriminator. GANs can craft all sorts of stuff. At the University of California, Berkeley, scientists built one that can turn images of horses into zebras or transform Impressionist paintings by the likes of Monet into crisp, photorealistic scenes.

Then, this past May, researchers at the Max Planck Institute for Informatics in Saarbrücken, Germany, and their colleagues revealed "deep video," which uses a type of GAN. It allows an actor to control the mouth, eyes and facial movements of someone else in prerecorded footage. Deep video currently only works in a portrait setup, where a person looks directly at the camera. If the actor moves too much, the resulting video has noticeable digital artifacts such as blurred pixels around the face.

GANs are not yet capable of building complex scenes in video that are indistinguishable from ones captured in real footage. Sometimes GANs produce oddities, such as a person with an eyeball growing out of his or her forehead. In February, however, researchers at the company NVIDIA figured out a way to get GANs to make incredibly high-resolution faces by starting the training on relatively small photographs and then building up the resolution step by step. And Hao Li's team at the University of Southern California has used GANs to make realistic skin, teeth and mouths, all of which are notoriously difficult to digitally reconstruct.

None of these technologies are easy for nonexperts to use well. But BuzzFeed's experiment hints at our possible future. The video came from free software called FakeApp—which used deep learning, though not GAN. The resulting videos are dubbed deepfakes, a mash-up of "deep learning" and "fake," named after a user on the Web site Reddit, who, along with others, was an early adopter and used the tech to swap celebrities' faces into porn. Since then, amateurs across the Web have used FakeApp to make countless videos—most of them relatively harmless pranks, such as adding actor Nicolas Cage to a bunch of movies he was not in or morphing Trump's face onto the body of German chancellor Angela Merkel. More ominous are the implications. Now that the technology is democratized, anyone with a computer can hypothetically use it.

CONDITIONS FOR FAKE NEWS

EXPERTS HAVE LONG WORRIED that computer-enabled editing would ruin reality. Back in 2000, an article in *MIT Technology Review* about products such as Video Rewrite warned that "seeing is no longer believing" and that an image "on the evening news could well be a fake—a fabrication of fast new video-manipulation technology." Eighteen years later fake videos don't seem to be flooding news shows. For one thing, it is still hard to produce a really good one. It took 56 hours for BuzzFeed to make the Obama clip with help from a professional video editor.

The way we consume information, however, has changed. Today only about half of American adults watch the news on television, whereas two thirds get at least some news via social media, according to the Pew Research Center. The Internet has allowed for a proliferation of media outlets that cater to niche audiences—including hyperpartisan Web sites that intentionally stoke anger, unimpeded by traditional journalistic standards. The Internet rewards viral content that we are able to share faster than ever before, Persily says. And the glitches in fake video are less discernible on a tiny mobile screen than a living-room TV.

The question now is what will happen if a deepfake with significant social or political implications goes viral. With such a new, barely studied frontier, the short answer is that we do not know, says Julie Carpenter, a research fellow with the Ethics + Emerging Sciences Group, based at California State Polytechnic University, San Luis Obispo, who studies human-robot interaction. It is possible we will find out soon enough, with key elections coming up this fall in the U.S., as well as internationally.

We have already witnessed the fallout when connectivity and disinformation collide. Fake news—fabricated text stories designed to look like legitimate news reports and to go viral—was a much discussed feature of the 2016 U.S. presidential election. According to collaborative research from Princeton University, Dartmouth College and the University of Exeter in England, roughly one in four Americans visited a fake news site during the five weeks between October 7 and November 14, 2016, mostly through the conduit of their Facebook feeds. Moreover, 2016 marked a low point in the public's trust in journalism. By one estimate, just 51 percent of Democrats and 14 percent of Republicans said they trusted mass media.

The science on written fake news is limited. But some research suggests that seeing false information just once is sufficient to make it seem plausible later on, says Gordon Pennycook, an assistant professor of organizational behavior at the University of Regina in Saskatchewan. It is not clear why, but it may be thanks to "fluency," he says, or "the ease at which it is processed." If we hear Obama call Trump a curse word and then later encounter another false instance where Obama calls Trump obscene names, we may be primed to think it is real because it is familiar.

According to a study from the Massachusetts Institute of Technology that tracked 126,000 stories on Twitter between 2006 and 2017, we are also more likely to share fake news than real news—and especially fake political stories, which spread further and quicker than those about money, natural disasters or terrorism. The paper suggested that people crave novelty. Fake news in general plays to our emotions and personal identity, enticing us to react before we have had a chance to process the information and decide if it is worth spreading. The more that content surprises, scares or enrages us, the more we seem to share it.

There are troubling clues that video may be especially effective at stoking fear. "When you process information visually, you believe that this thing is closer to you in terms of space, time or social group," says Elinor Amit, an assistant professor of cognitive, linguistic and psychological sciences at Brown University, whose work teases out the differences in how we relate to text and images. She hypothesizes that this distinction is evolutionary—our visual development came before written language, and we rely more on our senses to detect immediate danger.

"We will not win this game. It's just that we will make it harder and harder for the bad guys to play it."
—Alexei Efros *University of California, Berkeley*

Fake video has, in fact, already struck political campaigns. In July, Allie Beth Stuckey, a TV host at Conservative Review, posted on Facebook an interview with Alexandria Ocasio-Cortez, a Democratic congressional nominee from New York City. The video was not a deepfake but an old-fashioned splice of a real interview with new questions to make Ocasio-Cortez appear to flub her answers. Depending on your political persuasion, the video was either a smear job or, as Stuckey later called it in her defense, satire. Either way, it had 3.4 million views within a week and more than 5,000 comments. Some viewers seemed to think Ocasio-Cortez had bombed a real interview. "Omg! She doesn't know what and how to answer," one wrote. "She is stupid."

That all of this is worrying is part of the problem. Our dark ruminations may actually be worse for society than the videos themselves. Politicians could sow doubt when their real misdeeds are caught on tape by claiming they were faked, for example. Knowing that convincing fakes are even possible might erode our trust in all media, says Raymond J. Pingree, an associate professor in mass communications at Louisiana State University. Pingree studies how confident people are in their ability to evaluate what is real and what is not and how that affects their willingness to participate in the political process. When individuals lose that confidence, they are more likely to fall for liars and crooks, he says, and "it can make people stop wanting to seek the truth."

A GAME OF CAT AND MOUSE

TO A COMPUTER SCIENTIST, the solution to a bug is often just more computer science. Although the bugs in question here are far more complex than bad coding, there is a sense in the community that algorithms could be built to flag the fakes.

"There is certainly technical progress that can be made against the problem," says R. David Edelman of M.I.T.'s Internet Policy Research Initiative. Edelman, who served as a tech adviser under Obama, has been impressed by faked videos of the former president. "I know the guy. I wrote speeches for him. I couldn't tell the difference between the real and fake video," he says. But while he could be fooled, Edelman says, an algorithm might pick up on the "telltale tics and digital signatures" that are invisible to the human eye.

So far the fixes fall within two categories. One proves that a video is real by embedding digital signatures, analogous to the intricate seals, holograms and other features that currency printers use to thwart counterfeiters. Every digital camera would have a unique signature, which, theoretically, would be tough to copy.

The second strategy is to automatically flag fake videos with detectors. Arguably the most significant push for such a detector is a program from the Defense Advanced Research Projects Agency called Media Forensics, or MediFor. It kicked off in 2015, not long after a Russian news channel aired fake satellite images of a Ukrainian fighter jet shooting at Malaysia Airlines Flight 17. Later, a team of international investigators pegged the flight's downing on a Russian missile. The satellite images were not made with deep learning, but DARPA saw the coming revolution and wanted to find a way to fight it, says David Doermann, MediFor's former program manager.

MediFor is taking three broad approaches, which can be automated with deep learning. The first examines a video's digital fingerprint for anomalies. The second ensures a video follows the laws of physics, such as sunlight falling the way it would in the real world. And the third checks for external data, such as the weather on the day it was allegedly filmed. DARPA plans to unify these detectors into a single tool, which will give a point score on the likelihood that a video is fake.

These strategies could cut down on the volume of fakes, but it will still be a game of cat and mouse, with forgers imitating digital watermarks or building deep-learning tools to trick the detectors. "We will not win this game," says Alexei Efros, a professor of computer science and electrical engineering at U.C. Berkeley, who is collaborating with MediFor. "It's just that we will make it harder and harder for the bad guys to play it."

And anyway, these tools are still decades away, says Hany Farid, a professor of computer science at Dartmouth College. As fake video continues to improve, the only existing technical solution is to rely on digital forensics experts like Farid. "There's just literally a handful of people in the world you can talk to about this," he says. "I'm one of them. I don't scale to the Internet."

SAVING REALITY

EVEN IF EACH OF US can ultimately use detectors to parse the Internet, there will always be a lag between lies and truth. That is one reason why halting the spread of fake video is a challenge for the social media industry. "This is as much a distribution problem as it is a creation problem," Edelman says. "If a deepfake falls in the forest, no one hears it unless Twitter and Facebook amplify it."

When it comes to curbing viral disinformation, it is not clear what the legal obligations are for social media companies or whether the industry can be regulated without trampling free speech. Facebook CEO Mark Zuckerberg finally admitted that his platform has played a role in spreading fake news—although it took more than 10 months following the 2016 election. Facebook, after all, was designed to keep users consuming and spreading content, prioritizing what is popular over what is true. With more than two billion active monthly users, it is a tinderbox for anyone who wants to spark an enraging fake story.

Since then, Zuckerberg has promised to act. He is putting some of the burden on users by asking them to rank the trustworthiness of news sources (a move that some see as shirking responsibility) and plans to use AI to flag disinformation. The company has been tight-lipped on the details. Some computer scientists are skeptical about the AI angle, including Farid, who says the promises are "spectacularly naïve." Few independent scientists have been able to study how fake news spreads on Facebook because much of the relevant data has been on lockdown.

Still, all the algorithms and data in the world will not save us from disinformation campaigns if the researchers building fake-video technology do not grapple with how their products will be used and abused after they leave the lab. "This is my plea," Persily says, "that the hard scientists who do this work have to be paired up with the psychologists and the political scientists and the communication specialists—who have been working on these issues for a while." That kind of collaboration has been rare.

In March, however, the Finnish Center for Artificial Intelligence announced a program that will invite psychologists, philosophers, ethicists and others to help AI researchers to grasp the broader social implications of their work. And in April, Persily, along with Gary King, a political scientist at Harvard University, launched the Social Data Initiative. The project will, for the first time, allow social scientists to access Facebook data to study the spread of disinformation.

With a responsibility vacuum at the top, the onus of rooting out fake videos is falling on journalists and citizen sleuths. Near the end of the deepfake video of Obama and Peele, both men say: "Moving forward, we need to be more vigilant with what we trust from the Internet. It's a time when we need to rely on trusted news sources." It may have been a fake, but it was true. SA

MORE TO EXPLORE

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FROM OUR ARCHIVES

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scientificamerican.com/magazine/sa

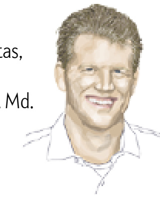
SEISMOLOGY

Earthquakes in the Sky

The best early warnings of a big disaster may appear 180 miles above the ground, a controversial new theory says

By Erik Vance

Illustration by María Corte



Science writer **Erik Vance** wrote about vaquitas, threatened porpoises in the Sea of Cortez, in the August 2017 issue. He lives in Baltimore, Md.

ON FRIDAY AFTERNOON, MARCH 11, 2011, KOSUKE HEKI WAS IN HIS OFFICE in Hokkaido University in northern Japan when the ground began to shake. The pulses were far apart, and each one lasted a few seconds. Heki, a geophysicist who studies an arcane phenomenon involving odd patterns formed by electrons in the sky after quakes, was interested but not unduly alarmed. It seemed like a large earthquake but far away. As the shaking continued, he thought perhaps data from the event might help his research. Then someone flipped on the news, and Heki's curiosity turned to horror.

The waves he felt had come from the biggest temblor in modern Japanese history—the devastating magnitude 9.0 Tōhoku earthquake, which cost the country hundreds of billions of dollars and claimed more than 15,000 of his compatriots' lives. The tsunami after the quake crippled the Fukushima Daiichi Nuclear Power Plant and triggered the worse nuclear disaster in a quarter of a century.

While emergency personnel worked to evacuate people and save lives in another part of the country, Heki could only wait for spotty phone and Internet service to come back online. By Sunday, the Internet was working, and he quickly downloaded satellite observations of the air over the region of Tōhoku and hungrily combed through them. As he expected, electrons in the ionosphere showed a disturbance 10 minutes after the quake. But he could not get his model to fit the data by just looking at the minutes after the quake. So he tried expanding the time frame, including the hour before. That is when he saw something that stopped him in his tracks.

Forty minutes *before* the earthquake struck, there was a subtle rise in electron density above the temblor's epicenter. Maybe it was an anomaly, a one-off or an instrument malfunction. Or maybe it was something more. Scientists have yet to find a reliable earthquake precursor—a telltale sign that could alert people before the onset of a large quake. If electron changes were such a warning, they could save thousands of lives a year.

Heki, whom colleagues describe as unassuming, quiet and cautious, was immediately skeptical of his own data, so he pulled up information from two other earthquakes. He saw the density change again and decided to keep digging. To date, he has found the electron signal before 18 big quakes, and over the past seven years he has come to believe it is real.

Other experts are now starting to take a close look at the idea. "Years ago people didn't think we could predict the weather, but we do now," says Yuhe Song, an expert in remote sensing at NASA's Jet Propulsion Laboratory. "We probably can see something earlier than when we feel it on the ground. There is something there … I think this warrants a discussion."

Not everyone agrees. Many scientists see Heki's work as the latest in a long line of false prediction promises. "These things are like the common cold: they're always going around," says seismologist Robert J. Geller, an emeritus professor at the University of Tokyo, who has spent years debunking various earthquake forecasting ideas. "If you ignore them, they go away."

Heki's idea seems to be sticking around, however, and may be getting stronger. The electron signal has shown up in medium-sized quakes as well as the largest ones. Other scientists have formed a theory that connects faults in the ground to activity in the sky. Heki has published his findings in reputable journals

IN BRIEF

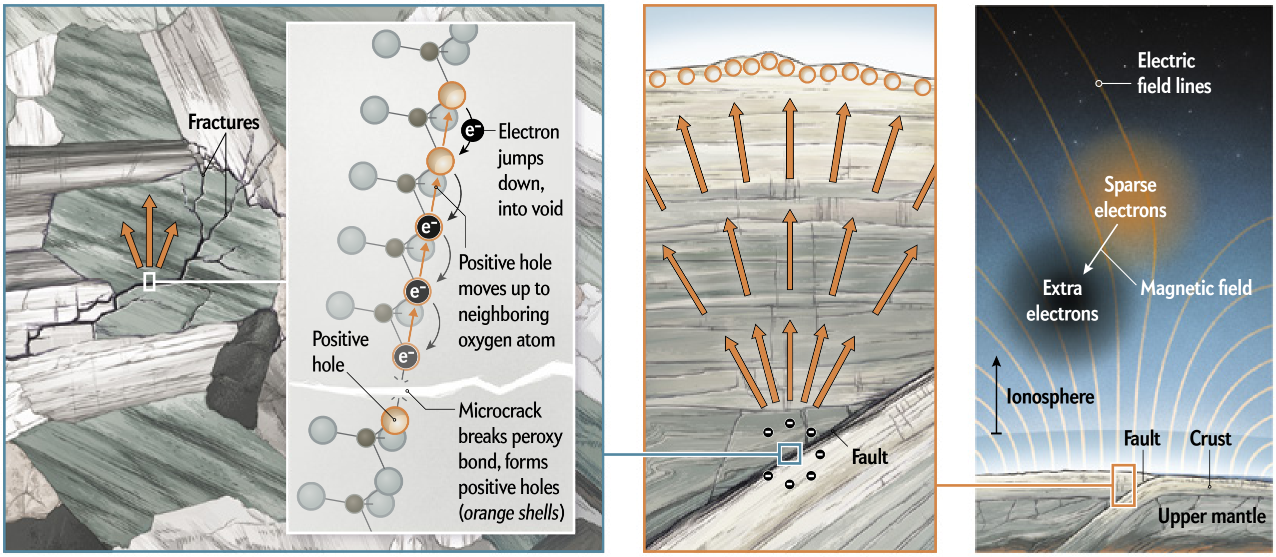
Tens of thousands of people can be killed by a single earthquake, so scientists have struggled to predict quakes well enough to sound an alarm.

New observations suggest that clumps of electrons form in the ionosphere, sometimes 30 minutes or more before a temblor, giving an early warning.

There have been false promises of prediction in the past, so this notion is drawing skeptics—but the data are beginning to convince more scientists.

From the Ground Up

Electrical disturbances miles above the planet's surface may occur at least half an hour before major earthquakes, new research indicates. These could be early warnings of disasters. And there is a theory about the way cracks in rocks might create activity high in the sky.



1. A Fracture Begins
Within the ground, parts of the earth's crust slide slowly across one another. Sometimes at a fault line they jerk suddenly, and the strain of the movement begins to tear the rock apart, creating small breaks called microfractures.

2. Electrons Jump
The microfractures generate enough force to break peroxy bonds, which hold together oxygen atoms within molecules in rock grains. This force alters the energy of negatively charged electrons in these grains, making the electrons move. They leave behind positively charged spaces called holes. As more electrons move, the holes move in the opposite direction, creating a tiny electric current in the rock grain.

3. To the Surface
This process continues across adjoining grains of rocks, like chains of falling dominos. Electrons move, leaving room for holes and their positive charges to propagate up from the original fracture, jumping from grain to grain up to the surface. Behind them, the strain created by grinding rocks grows.

4. Up in the Air
When positive holes accumulate at the surface, they can pull electrons from molecules there, generating an electromagnetic field. These fields can form lines that extend miles upward. They alter patterns of electrons in the ionosphere, making dense clumps in certain spots and sparse concentrations in others. Such anomalies can be detected by satellites.

such as *Geophysical Research Letters* and been invited to lecture about the results at the American Geophysical Union's annual meeting. This past spring Japan's Chiba University hosted an entire meeting to debate quake prediction, including his idea. If Heki is right, the implications for public safety are enormous, but there are difficult questions about how to use such a precursor. How accurate must a warning system be to sound an alarm, and what kind of emergency response should ensue?

PREDICTING THE WORST

CHARLES F. RICHTER—creator of the quake magnitude scale that carries his name—is said to have remarked that "only fools and charlatans predict earthquakes." But that hasn't stopped people from trying. In 373 B.C., animals reportedly ran for shelter five days before an estimated 6.0 to 6.7 magnitude temblor rocked Greece and destroyed the city of Helike. The Japanese once thought that twitching or thrashing catfish could predict earthquakes. Dogs, sheep, centipedes, cow's milk and a Sumatran pheasant called the great argus have all been said to change their behavior before a quake.

Others have looked at wells that suddenly go dry, temperature changes, radon gas emissions and, of course, groups of smaller foreshocks as possible precursors. In 1975, using a combination of these signs (including animal behavior), the Chinese even managed to predict a 7.3 quake early enough to begin evacuating the city of Haicheng. It raised hopes. "In the 1970s American and Japanese seismologists became pretty optimistic about short-term earthquake prediction," says Masao Nakatani, an expert in rock mechanics at the University of Tokyo. "We tended to believe that earthquakes must be predictable." By the 1980s both the U.S. and Japan had created research groups to pursue the challenge.

Reliable signals proved elusive, however. One year after the Chinese success the same techniques failed to spot another, larger quake that killed hundreds of thousands of people. Japan, sitting on the tectonically restless Ring of Fire around the Pacific, put in a fair amount of effort only to find that a precursor would work once and not again. Nature seemed to keep changing the rules. The U.S. abandoned forecasting efforts in the late 1990s after a predicted quake—based on the pattern of

Illustration by Matthew Twombly

previous earthquakes—failed to appear near Parkfield, Calif. (It eventually hit in 2004 but with none of the expected warning signs.)

The year of the Tōhoku quake, an international commission on prediction, set up by the Italian government, essentially closed the book on the field. "In spite of continuous research efforts in Japan, little evidence has been found for precursors that are diagnostic of impending large earthquakes," the members wrote in May 2011.

Four months later Heki reopened the book. What he saw were bizarre pockets of ionized particles not at or on the earth's surface but 186 miles above it. The idea of a connection between ground and sky is not out of this world. In the 1970s scientists first found that rocks under extra pressure create an electric current, like a very weak battery. The theory goes that as a rock is pressurized, its oxygen atoms give up electrons, leaving deficits that physicists describe as positive holes. Electrons from other nearby atoms move into those holes, leaving yet more holes behind them, creating a chain reaction of moving charges.

TOLL OF A QUAKE: With little warning, the deadly Tōhoku earthquake and tsunami destroyed the Japanese city of Rikuzentakata; afterward, residents walked among the ruins.

NICOLAS ASFOURI *Getty Images*

The holes "have the ability to move around over long distances—miles, tens of miles, hundreds of miles," says Friedemann Freund, a researcher at NASA and the SETI Institute, who discovered the phenomenon. "It's like a bucket of water in a fire line. It's being handed from person to person to person."

Freund says that the holes then roam through rocks, eventually reaching the earth's surface, where they attract negatively charged electrons from molecules in the air, like a magnet attracting iron shavings. The electrical charges then travel to the upper atmosphere. The mechanism is just theory because it is hard to measure directly, but it seems to fit with hints of electron clumps seen after an earthquake. But no one had clearly seen the effect *before* a quake.

For his research, Heki brought in a new method that used sophisticated GPS satellite networks, which can detect subtle changes in atmospheric electrons when their radio signals bend across the atmosphere. Japan has a particularly dense GPS receiver network, which allowed Heki to spot a subtle electron surge in the sky far above Tōhoku's epicenter, about 40 minutes before seismometers in the ground detected any movement.

But the geophysicist says he was reluctant to present his findings. "I had to worry about how to publish it," he says. "Earthquake prediction is something special. Everybody becomes very emotional."

He did not, in fact, publish right away. After Tōhoku, Heki looked back at two giant earthquakes where detailed GPS data were available. In each, he found a telltale rise in electron concentration more than 30 minutes beforehand. The larger the quake, the longer the advance time, it seemed. A magnitude 8.2 quake in 2014 in Chile had a 25-minute lead time, whereas 9.0 Tōhoku gave the 40 minutes. So the signals not only hinted that the faults were about to slip; they also indicated the relative size of the ensuing temblor. "I have never seen such a clear phenomenon occurring just before an earthquake," he says.

CHAOTIC DEBATE

ARMED WITH THESE DATA, Heki finally published a paper in September 2011, announcing what he found. Other scientists quickly started pointing out problems. Some said the result came from a misreading of the data and that disturbances during and after the quake muddied the picture. Heki responded by using a different analytical method to highlight the prequake effects. He also converted measurements taken at an angle to a bird's-eye view, thinking this would make the effects easier to spot. But critics argued this was just reorganizing the same flawed data. Another Japanese team said the effect was caused by geomagnetic storms. Heki performed another analysis to account for storm effects and found that storms could not explain all the changes he saw.

Soon some doubters began to agree with him. "This is by far the best precursor ever reported," says Nakatani, who says he stopped believing in earthquake forecasting after the failures of the 1990s. But Heki has rekindled his faith, so much so that he now says the work could very well be "the most important discovery in the history of earthquake science." NASA's Song is less hyperbolic but agrees the electron clouds have been hard to explain away as errors and seem to signify a real event. Freund says Tōhoku followed months of pressure buildup and changes in electron density. And although that pressure might have found other outlets—such as invisible "silent" earthquakes—the charged particle release is still a predictable phenomenon that, in theory, could be detected in other quakes.

Critics, however, insist Heki is seeing things in a computer that do not exist in the real world. "He is trying to confirm his initial thought without providing a valid support," says Fabrizio Masci of the National Institute of Geophysics and Volcanology in Italy. He has published papers refuting not just Heki but other earthquake prediction ideas and says Heki's responses are "a skillful way to distract the reader." Many of the criticisms focus on Heki's reading of baseline electron levels. The tiny particles permeate our planet and fluctuate as much as the weather. Heki says that just before an earthquake, electrons clump a little more than average. Critics say that the change is caused by the daily ebb and flow of electrons. In other words, Heki may be chasing a statistical ghost.

Masci goes even further and says seismic precursors might be impossible if earthquakes themselves are fundamentally chaotic. If the initial conditions of an event are not precisely determined, it is impossible to know how the effects will play out. And with quakes, it is devilishly hard to nail down all the initial conditions.

Giovanni Occhipinti of the Institute of Earth Physics of Paris is not so pessimistic, although he agrees it is a daunting problem to understand all the factors at play—the rock type, the pressure, the faults nearby—well enough that you can make a prediction. Occhipinti, like Heki, studies how earthquakes affect atmospheric ions. He says that, given how chaotic ions are in the atmosphere, you simply cannot pull a signal from all the noise. It is like trying to predict a hurricane based on a single cloud a day beforehand. "The problem is there are tons of clouds that are coming and moving around," he says. "It's not simple to deduce a way to discriminate that specific cloud that you want to see as a precursor."

> **"It's pushing science forward," but "you have to be really, really, really precise. You are playing with the lives of people."**
>
> —Giovanni Occhipinti *Institute of Earth Physics of Paris*

Until recently, Occhipinti was on the side of skeptics and felt that Heki's discovery was merely a statistical hiccup. Heki's latest work, however, which takes into account the complex 3-D space in which the effects happen, caught his interest. Rather than a limited satellite snapshot, 3-D modeling shows multidimensional effects that point to a consistent physical process underlying the anomalies, making them hard to write off as ghosts. Occhipinti wants to see more 3-D analyses, along with comparisons of those results with other models to see how well they fit. So he is not, as yet, a complete believer. But he calls the idea "intriguing" and is now looking into it more closely. "It's pushing science forward," Occhipinti says, but "you have to be really, really, really precise. You are playing with the lives of people."

SOUNDING ALARMS

THE NUMBERS OF THOSE LIVES can reach into the hundreds of thousands. The U.S. Geological Survey examined worldwide earthquake fatalities for a 16-year period beginning in 2000. The death counts fluctuate because there are not giant quakes every year. But the toll is daunting. In seven of those years there were more than 20,000 deaths, and for another two years the totals exceeded 200,000. In the countries hardest hit, people are desperate for any kind of warning, even just a few seconds. Take Mexico City, one of the most lethal and well-studied earthquake zones on the planet. After a devastating 1985 quake that killed as many as 10,000 people, the government took advantage of the fact that quake waves travel over unusually long distances in the region and built a monitoring system that can give a couple of minutes warning if the waves are detected far enough away.

Carlos Valdés, a geophysical engineer and director of Mexico's National Center for Prevention of Disasters, says a 40-minute warning might sound good, but the reality is not so simple. First, false alarms can ruin any emergency response. Some Mexican quakes triggered warnings but were too weak or in the wrong position to actually shake the city, for instance. People became annoyed and stopped responding to those alerts. But he worries more about the opposite problem: panic. "Somebody is going to say, 'I have 40 minutes, I'm going to leave the city,'" he says. "It takes only one person to start screaming or start running, and everyone follows." Roads clog, and no one gets to safety [see "This Way Out," on page 74].

Still, other emergency planners note that even short warning times create the opportunity to shut down gas lines or stop subways, reducing risks. And greater accuracy would solve the false alert problem. British and Russian scientists have proposed a satellite that could better track atmospheric anomalies such as the ones Heki studies, and China is moving forward with a space-based prediction program that relies on electromagnetic disturbances in the ionosphere. But given the complex nature of the ionosphere, coupled with the confusing nature of earthquakes, it may be decades until atmospheric data become actual earthquake warnings.

Geller does not think that day will ever come. "The precursor hunters throughout the past 130 years have a childlike belief that, one, there must be precursors and that, two, the bigger the quake, the bigger the precursors must be. But there's no particular reason these beliefs should be correct," he says.

Still, Heki is moving forward. He recently published a paper that analyzes the precursor of a 2015 Chilean quake in detailed 3-D, which he says may make his ideas harder to refute. He is also trying to fill in some data gaps between the electrical charges and the actual earthquake locations themselves. The goal is to better understand what it is in the crust that creates the effects high above. "There is something before an earthquake in the ionosphere. I don't know about a physical mechanism," Heki says, "but the observation itself is so clear." SA

MORE TO EXPLORE

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FROM OUR ARCHIVES

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STATE OF THE WORLD'S SCIENCE 2018

HOW TO FIX SCIENCE

WHETHER OR NOT THERE IS AN ACTUAL "WAR ON SCIENCE" UNDER WAY, A MILLION supporters of evidence-based thinking felt threatened enough to show up to the global 2017 March for Science. President Donald Trump has called global warming a "hoax," and his administration has canceled, blocked and defunded scientific efforts to protect the environment and public health. Moreover, climate change denial is not restricted to the U.S., and dozens of countries have banned the cultivation of GMO crops, despite evidence that genetically modified foods are just as safe as traditionally bred varieties.

There are many ways to fight back, including improving education, outreach and political reform. But science must also tackle its own problems, from how we fund it to how we treat young scientists, ensure reproducible results, curb sexual harassment and encourage interdisciplinarity. Some creative solutions are already showing promise on these fronts, but science must fortify itself to withstand the current assault.

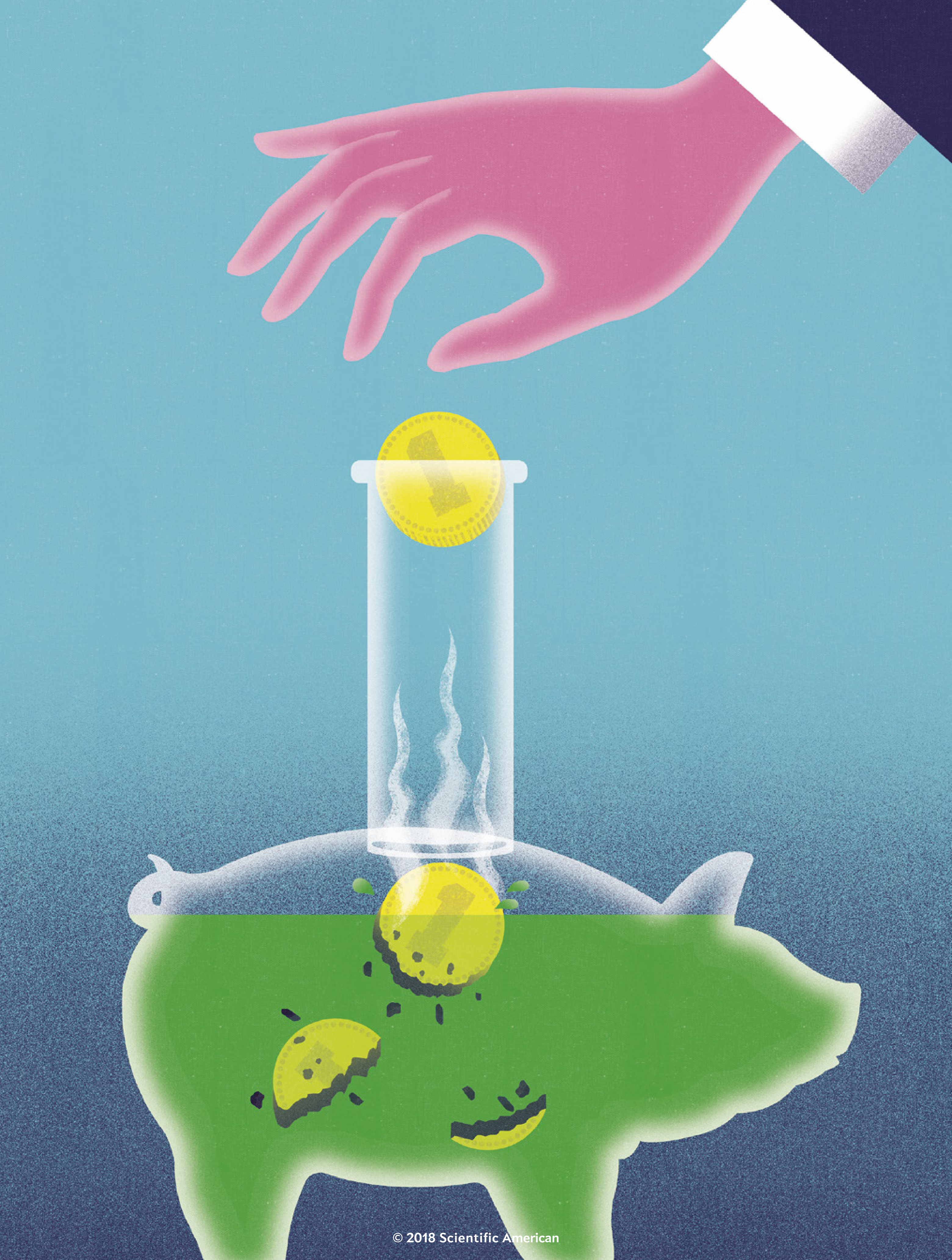
IN BRIEF

To weather antiscience currents, scientists must shore up their enterprise from the inside.

The way research is funded is inefficient and often leads to poor results. Too many findings fall apart under scrutiny and fail the reproducibility test. Sexual harassment is a crisis that threatens all of science.

Life is too hard for young scientists, who face unnecessary hurdles finding jobs and funding and starting families on academic time lines. And too many scientists are isolated from like-minded colleagues in other disciplines.

Illustration by Neil Webb



STATE OF THE WORLD'S SCIENCE 2018

RETHINK FUNDING

The way we pay for science does not encourage the best results

By John P. A. Ioannidis

Illustration by Neil Webb

John P. A. Ioannidis is a professor of medicine, of health research and policy, of biomedical data science and of statistics at Stanford University. He is also co-director of the Meta-Research Innovation Center at Stanford (METRICS).

WITH MILLIONS OF SCIENTIFIC PAPERS published every year and more than $2 trillion invested annually in research and development, scientists make plenty of progress. But could we do better? There is increasing evidence that some of the ways we conduct, evaluate, report and disseminate research are miserably ineffective. A series of papers in 2014 in the *Lancet,* for instance, estimated that 85 percent of investment in biomedical research is wasted. Many other disciplines have similar problems. Here are some of the ways our reward and incentives systems fail and some proposals for fixing the problems.

We Fund Too Few Scientists

Funding is largely concentrated in the hands of a few investigators. There are many talented scientists, and major success is largely the result of luck, as well as hard work. The investigators currently enjoying huge funding are not necessarily genuine superstars; they may simply be the best connected.

Solutions:

— Use a lottery to decide which grant applications to fund (perhaps after they pass a basic review). This scheme would eliminate the arduous effort and expenditure that now goes into reviewing proposals and would give a chance to many more investigators.

— A proposed cap to the maximum funding that any single investigator can receive was fiercely shot down by the prestigious institutions that gain the most from this overconcentration. Shifting the funds from senior people to younger researchers, perhaps even in the same laboratory, however, would not affect these institutions and would also make the cohort of principal investigators more open to innovation.

We Do Not Reward Transparency

Many scientific protocols, analysis methods, computational processes and data are opaque. When researchers try to crack open these black boxes, they often discover that many top findings cannot be reproduced. That is the case for two out of three top psychology papers, one out of three top papers in experimental economics and more than 75 percent of top papers identifying new cancer drug targets. Most important, scientists are not rewarded for sharing their techniques. These good scientific citizenship activities take substantial effort. In competitive environments, many scientists even think, Why offer ammunition to competitors? Why share?

Solutions:

— Create better infrastructure for enabling transparency, openness and sharing.

— Make transparency a prerequisite for funding.

— Universities and research institutes could preferentially hire, promote or tenure those who are champions of transparency.

We Do Not Encourage Replication

Under continuous pressure to deliver new discoveries, researchers in many fields have little incentive and plenty of counterincentives to try replicating results of previous studies. Yet replication is an indispensable centerpiece of the scientific method. Without it, we run the risk of flooding scientific journals with false information that never gets corrected.

Solutions:

— Funding agencies must pay for replication studies.

— Scientists' advancement should be based not only on their discoveries but also on their replication track record.

We Do Not Fund Young Investigators

The average age of biomedical scientists receiving their first substantial grant is 46 and is increasing over time. The average age for a full professor in the U.S. is 55 and growing. Only 1.6 percent of funding in the NIH's Research Project Grant program went to principal investigators younger than 36 in 2017, but 13.2 percent went to those 66 and older. Similar aging is seen in other sciences, and it is not explained simply by life-expectancy improvement. Werner Heisenberg, Albert Einstein, Paul Dirac and Wolfgang Pauli made their top contributions in their mid-20s. Imagine telling them it would be another 25 years before they could receive funding. Some of the best minds may quit rather than wait.

Solutions:

— A larger proportion of funding should be earmarked for young investigators.

— Universities should try to shift the aging distribution of their faculty by hiring more young investigators.

We Use Biased Funding Sources

Most funding for research and development in the U.S. comes not from the government but from private, for-profit sources, raising unavoidable conflicts of interest and pressure to deliver results favorable to the sponsor. Clinical trials funded by the pharmaceutical industry, for instance, have 27 percent higher odds of reaching favorable results than publicly funded trials. Some of the sponsors are improbable champions of scientific truth. For example, Philip Morris (the manufacturer of Marlboro cigarettes) recently announced it would contribute $960 million over 12 years to establish the Foundation for a Smoke Free World, a nonprofit initiative that aims to eliminate smoking. Disclosure of conflicts of interest has improved in many fields, but in-depth detective work suggests that it is still far from complete.

Solutions:

— Restrict or even ban funding that has overt conflicts of interest. Journals should not accept research with such conflicts.

— For less conspicuous conflicts, at a minimum ensure transparent and thorough disclosure.

We Fund the Wrong Fields

Much like Mafia clans, some fields and families of ideas have traditionally been more powerful. Well-funded fields attract more scientists to work for them, which increases their lobbying reach, fueling a vicious circle. Some entrenched fields absorb enormous funding even though they have clearly demonstrated limited yield or uncorrectable flaws. Further investment in them is futile.

Solutions:

— Independent, impartial assessment of output is necessary for lavishly funded fields.

— More funds should be earmarked for new fields and fields that are high risk.

— Researchers should be encouraged to switch fields, whereas currently they are incentivized to focus in one area.

We Do Not Spend Enough

In many countries, public funding has stagnated and is under increasing threat from contesting budget items. The budget for U.S. military spending ($886 billon) is 24 times the budget of the NIH ($37 billion). The value of a single soccer team such as Manchester United ($4.1 billion) is larger than the annual research budget of any university. Investment in science benefits society at large, yet attempts to convince the public often make matters worse when otherwise well-intentioned science leaders promise the impossible, such as promptly eliminating all cancer or Alzheimer's disease. When these promises do not deliver, support for science can flag.

Solutions:

— We need to communicate how science funding is used by making the process of science clearer, including the number of scientists it takes to make major accomplishments. Universities, science museums and science journalism can help get this message out.

— We would also make a more convincing case for science if we could show that we do work hard on improving how we run it.

We Reward Big Spenders

Hiring, promotion and tenure decisions primarily rest on a researcher's ability to secure high levels of funding. But the expense of a project does not necessarily correlate with its importance. Such reward structures select mostly for politically savvy managers who know how to absorb money.

Solutions:

— We should reward scientists for high-quality work, reproducibility and social value rather than for securing funding.

— Excellent research can be done with little to no funding other than protected time. Institutions should provide this time and respect scientists who can do great work without wasting tons of money.

We Do Not Fund High-Risk Ideas

Review panels, even when they are made up of excellent scientists, are allergic to risky ideas. The pressure that taxpayer money be "well spent" leads government funders to back projects most likely to pay off with a positive result, even if riskier projects might lead to more important, but less assured, advances. Industry also avoids investing in high-risk projects, waiting for start-ups to try (and often fail with) out-of-the-box ideas. As a result, nine out of the 10 largest pharmaceutical companies spend more on marketing than on R&D. Public funding agencies contend that they cherish "innovation" when they judge grant applications. This is nonsense. Innovation is extremely difficult, if not impossible, to predict in advance. Any idea that survives the scrutiny of 20 people reviewing it (the typical NIH study section) has little chance of being truly disruptive or innovative. It must be mainstream, if not plain mediocre, to be accepted by everyone.

Solutions:

— Fund excellent scientists rather than projects and give them freedom to pursue research avenues as they see fit. Some institutions such as Howard Hughes Medical Institute already use this model with success.

— Communicate to the public and policy makers that science is a cumulative investment. Of 1,000 projects, 999 may fail, and we cannot know which one will succeed ahead of time. We must judge success on the total agenda, not a single experiment or result.

We Lack Good Data

There is relatively limited evidence about which scientific practices work best. We need more research on research ("meta-research") to understand how to best perform, evaluate, review, disseminate and reward science.

Solution:

— We should invest in studying how to get the best science and how to choose and reward the best scientists. We should not trust opinion (including my own) without evidence.

STATE OF THE WORLD'S SCIENCE 2018

MAKE RESEARCH REPRODUCIBLE

Better incentives could reduce the alarming number of studies that turn out to be wrong when repeated

By Shannon Palus

Illustrations by Neil Webb

KATIE CORKER WONDERED what temperature the coffee was supposed to be. She was doing a psychology experiment—well, redoing an experiment. The original findings, suggesting that holding something warm can make a person behave warmly, had been published in 2008 in the prestigious journal *Science* to a flurry of media coverage. Yet as Corker tried to retrace each step in the study, there were so many unknowns: the temperature of the hot coffee distributed to subjects, how quickly the mug cooled in their hands.

Corker, a psychologist at Grand Valley State University, was trying what few scientists attempt: to carefully replicate research and publish the results. The goal, in her case, was to find out whether she, working in another laboratory with a different group of subjects, would find the same effect as the *Science* study, which had been conducted by just one research group with only 94 participants clutching coffee or therapeutic pads of varying temperatures. In theory, this is how science is supposed to work: as a self-correcting process in which researchers build on the findings of others.

For decades it has been something of an open secret that a chunk of the literature in some fields is plain wrong. In biomedicine, the truth became clear in 2012. At the time, C. Glenn Begley was a vice president and global head of hematology and oncology research at the pharmaceutical company Amgen, overseeing the development of cancer drugs based, in part, on promising breakthroughs from academia. After a decade in the gig, he wanted to know why some projects looking into promising targets for drugs were being halted. He turned to the company's files and found that, incredibly, often the problem lay with the preclinical research, something that his teams double-checked before pouring money and resources into basing a treatment on it. "To my horror, I discovered that 90 percent of the time, we were unable to reproduce what was published," says Begley, who is now CEO of the Australian firm BioCurate. A study would later find that failures to replicate preclinical work in the field of biomedicine eat up $28.2 billion every year in the U.S. Begley even sent Amgen scientists to some labs to watch them try to replicate their own results. They failed, too.

Meanwhile the crisis was becoming apparent in psychology. Nearly 300 scientists were volunteering their time to repeat experiments in 100 papers in the field as part of University of Virginia psychologist Brian Nosek's Reproducibility Project: Psychology. In 2015 they declared that just 36 percent of the repeated experiments showed significant results in line with the original findings.

Although the landmark reproducibility studies have been in biomedicine and psychology, the issue is not confined to those fields. Lorena A. Barba, an engineer at George Washington University, who works in computational fluid dynamics, spent a full three years collaborating with a student to reconstruct a complex simulation from her own lab on how flying snakes, which leap off tree branches to glide through the air, wiggle as they soar. The new results were consistent, but she learned that sifting through other people's code to piece together what they did can be a nightmare. She essentially encountered the same problem that Corker did with the hot cups of coffee. Scientists are focused on publishing results, not necessarily on every mundane step of how they arrived at them. "There's just not a lot written down," Corker says. She got lucky, though: the original first author of the coffee study was "very willing to work with us." She also collaborated with a chemist to standardize how quickly the test apparatus changed temperature. "I found it more challenging than some of the original research I've done," she says.

Long-ingrained scientific habits such as an aversion to sharing techniques for fear of being scooped often work counter to the goal of reproducibility. Barba's own field was born in a veil of secrecy in Los Alamos, N.M., during the Manhattan Project, as researchers designing the first nuclear weapons used early computers to calculate how blasts of air and energy would ripple off exploding bombs. The Manhattan Project, of course, provided fuel to large swaths of the hard sciences. Scientists at the time actively tried to prevent outsiders from replicating their work.

Furthermore, journals and tenure committees often prize new, flashy results instead of piecemeal advances that carefully build on the existing literature. "My training was about trying to find the unexpected effect," says Charlotte Tate, a social and personality psychologist at San Francisco State University. She jokes that members of her field "run around with this model that we have to get on the *Daily Show*." This attitude is not just vanity: flashy results are often how you secure a job. Those quietly fact-checking the work of others or spending extra hours toiling to ensure that their code is easy for another researcher to understand do not earn a name in lights—or even at the top of a stack of resumes.

Many emphasize the role that better training—on how to write a bullet-proof "methods" section of a paper or carefully document code so that it is legible to others—can play in helping

seeking grant money to improve the reproducibility of their work. The NIH now asks for more information about how the study builds on previous work and a list of variables that could impact the investigation, such as the sex of rat subjects (a previously overlooked factor that led many studies to describe phenomena found in male rats as universal).

And all the questions that a funder can ask up front could also be asked by journals and reviewers. For Nosek, a promising solution lies in what is known as registered reports, a preregistration of studies in which scientists submit research analysis and design plans for publication before they actually do it. Peer reviewers then evaluate the methodology—if it is sound, if it builds on past findings—and the journal promises to print the results no matter what they are. The reward of a paper comes for carefully thought-out experiments, not flashy results. Some wonder if such a change would simply produce boring science. Nosek contends that is not the case. He is currently completing a pair of investigations to examine the impact and quality of the early registered reports that have been published; preliminary results suggest that they are cited just as often as traditional papers. Still, he notes that relying too heavily on preregistered studies could encourage safer research, potentially overcorrecting the problem. He sees the model operating in tandem with the traditional results-focused model, one that is friendly to haphazard discoveries, the "accidental arrival of things," he says.

A harder problem to solve is the pressure for researchers to produce breakthroughs to make a living. A larger cultural shift would need to take place, Nosek notes. Right now it is not necessarily enough to carefully trod down intriguing paths that turn out to be empty, expanding the map of knowledge by illuminating the dead ends. We do not live in a world where fact-checkers become famous.

Yet the reproducibility problem does not necessarily mean that science is fundamentally broken. "Progress is dependent on failures," says Richard M. Shiffrin, a psychologist at Indiana University Bloomington, who is skeptical of the attention being paid to the "crisis." He argues that focus on irreproducibility stands to overshadow the advances that science has brought us. Those who do see the crisis as real do not always disagree with his assessment. Begley notes that the problem has real consequences: so many findings fail under scrutiny that drugs are arriving slower and at higher costs than they would under a cleaner system. "We spend a lot of time chasing red herrings," he says.

The effects in the coffee study turned out to be one of them. Corker's work, which she completed with hot and cold pads, ultimately showed there was no evidence that holding something warm could make you act warmer. Although the original work appeared in a topflight journal, the replication effort can be found in a comparatively smaller one. It was a breakthrough of a different kind, one met with less pizzazz.

the crisis. Barba is in this camp, noting that people who use code in their work would do well to take a software etiquette class so that they can present well-documented code alongside their results. She also uses a technology known as version control, which records any changes made to a file, to make the evolution of her team's code as legible as possible. The tool is standard in software development but, bafflingly to Barba, not yet in science. "There's this fundamental tension between doing an experiment and documenting the experiment," says Charles Fracchia, who is trying to increase the detail and depth of experiment logs in biomedicine through his company BioBright. One of his tools, DarwinSync, records data from every instrument possible, including seemingly unimportant things such as whether a computer was plugged in or running on a battery or the amount of ambient light in a room, in case those details are later revealing. In the case of Corker's replication attempt, if the original study had better assessed the mugs' temperatures, that would have set her up with more information to rerun the trial later.

But time-intensive solutions and expensive equipment are not enough. "There's no reward for doing things right," Barba says. The trick, Nosek says, is to rework the incentives to ensure "what's good for a scientist is what's good for science." For instance, agencies that fund research could choose to finance only projects that include a plan for making their work transparent. In 2016 the National Institutes of Health rolled out new application instructions and review questions to encourage scientists

Shannon Palus is a freelance journalist and staff reporter at Wirecutter, which is part of the New York Times Company. Her work has appeared in Slate, *Popular Science,* the *Atlantic, Discover, Audubon,* Quartz, *Smithsonian* and Retraction Watch.


STOP

STATE OF THE WORLD'S SCIENCE 2018

END HARASSMENT

A leader of a major report on sexual misconduct explains how to make science accessible to everyone

By Clara Moskowitz

SEXUAL HARASSMENT is more prevalent in academia than in any sector of society except the military. According to a groundbreaking June report by the National Academies of Sciences, Engineering, and Medicine, harassment hurts individuals, diminishes the pool of scientific talent and ultimately damages the integrity of science itself. To understand the problem and how best to tackle it, a committee of 21 experts spent two years surveying existing data and commissioning new research. During that time, the #MeToo movement awoke the world to the prevalence of sexual harassment and the devastation it causes. Now ***Paula Johnson,*** *president of Wellesley College and co-chair of the committee behind the report, hopes its recommendations will fall on ears ready and willing to heed its advice. SCIENTIFIC AMERICAN spoke to Johnson about how to move forward. An edited transcript of the conversation follows.*

What do we need to do to change the situation?

We found the policies and procedures that are in place are not preventing sexual harassment. We know that you have to go on a path of culture change. We've identified some major areas that have to be addressed. One is creating a diverse, inclusive and respectful environment. Another is really changing the power dynamics in adviser-trainee relationships. We need to make them less singular, to consider group mentoring, and to think about ways you might uncouple the mentoring relationship from financial dependence on the mentor. The third is supporting the targets of harassment, providing alternative ways to access services, whether or not they decide to report.

There are also certain structural aspects of the way we handle cases now that really work against what we're trying to achieve. For example, we made a recommendation that confidentiality agreements with perpetrators be prohibited. They prevent institutions from being transparent and inhibit them from being able to provide information that could be important to other institutions.

You also found that only a minority of people who experience harassment report it. How can we change that?

There are some novel approaches for reporting experiences of harassment that provide more control to the target. One is a program called Callisto that's now being adopted by a growing number of colleges and universities. It allows people to go in and record if an experience of harassment occurred and time-stamp it, without actually formally reporting it. People can see if others have recorded experiences with the same accused harasser. It allows people to share data in an anonymous way. It's a very hopeful, interesting tool.

Did the report address how harassment affects women of color and other minority groups differently?

We found women of color experience more harassment than do white women, white men and men of color. And that women of color also experience racial and ethnic harassment.

We crafted our recommendations with this finding in mind. Creating a more diverse, inclusive, respectful environment—that will help address this issue.

Your background is in medicine, which is the field within science where harassment is most prevalent. Why do you think that is?

The qualitative interview research commissioned by the committee provided some insight. It showed that with some of the expectations of grueling conditions in [medical] training, several respondents viewed sexual harassment as just part of the continuum of what they were expected to endure. Targets might say, "This is a really tough experience, and the conditions are pretty difficult, and [harassment] is part of that."

Are you optimistic that the changes you call for will take place?

I am. We all know that culture change is not easy and that it doesn't happen overnight. But neither did this problem arise overnight. We've seen leaders, myself included and many others, who are already taking the initiative to pursue some of the changes that we've suggested. Obviously, the fact that harassment is so prevalent is alarming. But we are providing a road map for a way forward, and I find that hopeful. And we're in a particular moment where I think we've got the will.

Clara Moskowitz is a senior editor at *Scientific American.*

Illustration by Neil Webb

HELP YOUNG SCIENTISTS

Life is hard for early-career researchers, who must contend with uncertain futures, compete for funding and balance family life, with the frequent need to move for jobs *By Rebecca Boyle*

Jennifer Harding was in her fourth year as a doctoral student at the University of Texas at Austin when the 2018 federal budget was finalized. A marine geophysicist, she had spent years training to use a National Science Foundation–funded research vessel to image subduction zones underneath the seafloor. Then she learned the NSF planned to sell the vessel, cutting off her access to new data. At 26 and in her final year of graduate school, Harding is trying to decide what to do next and expects she may have to find a job in the oil and gas industry. "The rug is being pulled out from under me," Harding says.

Young scientists such as Harding run a gauntlet that begins as soon as they don their undergraduate commencement caps. They cope with moving across countries, continents or oceans for Ph.D. programs, postdoctoral appointments or professorships. They contend with long-distance relationships and family stresses, including agonizing over when or whether to have children despite their uncertain future. They compete for scarce funding. Some leave academia for industry careers, which present their own set of challenges and, some argue, have a negative reputation among academics. And these are all problems that face those fortunate enough to be accepted into graduate research programs in the first place.

Early-career research is in dire need of reforms, asserts an April report by the National Academies of Sciences, Engineering, and Medicine. According to the report, in 2016 the average researcher was 43 years old before securing his or her first independent grant from the National Institutes of Health, compared with an average age of 36 in 1980.

Several scientists shared with us their most common frustrations, struggles, challenges—and joys.

Rebecca Boyle is an award-winning freelance journalist. She is a contributing writer for the *Atlantic*, and her work regularly appears in *New Scientist, Wired, Popular Science* and other publications.

MOVING

Ashley Juavinett, *28,* postdoctoral researcher in neuroscience at Cold Spring Harbor Laboratory

"So few people within academia talk about it because it's so expected: 'Of course, you'll move across the country for a postdoc because that's what everybody does.' The move definitely took a toll on my relationship. My partner is in the Bay Area. There was, for a long time, this question of whether she should move to New York instead. It's a hard call, especially in a same-sex couple. We don't know whose career comes first."

MONEY

Alexis Weinnig, *28,* third-year Ph.D. student in biology at Temple University

"We work probably between 60 and 80 hours a week, and we get paid at a salary of probably 25 hours a week. The system has just not kept up with the cost of living. I love what I'm doing, but I would also like to be compensated for the level of work that I'm doing."

Save Kumwenda, *41,* Ph.D. student in epidemiology at the University of Malawi

"The biggest challenge is to get funding, let alone enough funding. Most grants assume that the institutions where you are applying from have some basic infrastructure, especially related to research involving the lab. But when you get the funding, it is not enough, because most of the equipment is not available and if it is available, it is outdated. Using it makes your results questionable and difficult to publish in high-impact journals."

Illustrations by Lara Tomlin

CULTURE

Skylar Bayer, *32,* marine ecologist and 2018 John A. Knauss Marine Policy Fellow

"A lot of the way science is set up is still very feudal. As a student, the person in charge of you is your adviser. If you don't have a good relationship with your adviser, you're screwed. There's not a lot of accountability. You are not a paid employee, so you don't have the same rights. You kind of need champions who can throw their weight around for you."

INDUSTRY VS. ACADEMIA

Maryam Zaringhalam, *30,* molecular biologist and AAAS Science & Technology Policy Fellow

"I knew pretty early on that I didn't want an academic career and learned to deal with a sense of shame about that. As an Iranian woman in science, I felt an obligation to continue down the pipeline because I know it's a leaky one. But I kind of resent the idea of a leaky pipeline at all because it privileges academic trajectories. There is a lot of space for people who have an academic background to go into careers in policy, advocacy, communication or industry, but those are looked down on as alternative."

FAMILY

Jacque Pak Kan Ip, *35,* postdoctoral researcher in neuroscience at the Massachusetts Institute of Technology

"We are planning to have kids. I cannot ask my wife to sacrifice her career again. But it has taken me a lot of time to do my research already. When she is pregnant and might need help, I might need to dial it back to help her. So we hesitate. A tenure-track position would be much more stable. Maybe at that time, we could plan to have a child. But then, I am 35; she is 34. The time window is getting narrower for us to have children."

Daniel Gonzales, *27,* NSF Graduate Research Fellow in Applied Physics at Rice University

"To be competitive on the academic job market one day, I need to continue on a path of ultraexcellence. I already have a publication in a high-impact journal, but I better get one more out before I graduate. I better choose a prestigious postdoctoral research position, not [here] in Texas. I better receive awards as a postdoc. I better continue to publish flashy science in top journals as a postdoc. But I have a family; I have two kids (one and three years old). Moving is hard, and working on a postdoc salary is hard. I know I have what it takes, but what will be the toll on my family?"

GETTING JOBS, FELLOWSHIPS OR INTO SCHOOL

Sophia Nasr, second-year Ph.D. student in cosmology at the University of California, Irvine

"The most devastating experience I ever had was applying for an NSF fellowship. I put my whole heart into it. I think my application was solid, and it just took one reviewer to flush it all down the drain. I found out right in the middle of my qualifying exams, so it was just crushing to my confidence. I've bounced back from that, but as a theorist, it's kind of hard to look for other places that will even offer me funding. For me, the NSF was where it was at, so it was heartbreaking."

Sneha Dharwadkar, *30,* wildlife biologist in Maneri, India

"Right now I am applying for Ph.D. programs in the U.S., and I am getting rejections. Most of the professors are telling me, 'You need to have publications before getting into a Ph.D. program.' But I am not in academia yet, so it is very hard to get a proper publication."

Carina Fish, *26,* second-year Ph.D. student in marine biogeochemistry at the University of California, Davis

"As someone who studies climate and the ocean, I used to get worked up that I wasn't doing enough to relieve some of the systemic and institutional racism my community faces. I was able to reconcile that by looking for the intersection of the two. I see my calling to be an advocate for environmental justice, especially given that climate change is exacerbating lots of social inequities."

Angel Adames-Corraliza, *29,* assistant professor of atmospheric sciences at the University of Michigan

"I am Puerto Rican, and there are so few of us in the science community that I feel like I have to represent my people. I want to pave the way for future generations of Latinos and Puerto Ricans and other underrepresented minorities. If I am faculty, I am at a certain position of power, so I can advocate for diversity in science and women in science."

Jack Nicoludis, *28,* postdoctoral fellow in biochemistry at the University of California, San Francisco

"As a postdoc, I'm likely going to apply to faculty positions. As a queer scientist, that's something I am a little unsure about. The mantra is that you apply to as many as you can. But these might be in states that don't recognize sexual orientation as a protected identity. I will have to decide whether I can see myself living in a place that might not be tolerant of my sexual orientation, because it might be the only place I can get a job."

STATE OF THE WORLD'S SCIENCE 2018

BREAK DOWN SILOS

Solving today's complex, global problems will take interdisciplinary science

By Graham A. J. Worthy and Cherie L. Yestrebsky

Illustration by Neil Webb

Graham A.J. Worthy is founder and director of the National Center for Integrated Coastal Research at the University of Central Florida (UCF Coastal) and chairs the department of biology. His research focuses on how marine ecosystems respond to natural and anthropogenic perturbations.

Cherie L. Yestrebsky is associate director of UCF Coastal and chairs the department of chemistry. Her research expertise is environmental chemistry and remediation of pollutants in the environment.

THE INDIAN RIVER LAGOON, a shallow estuary that stretches for 156 miles along Florida's eastern coast, is suffering from the activities of human society. Poor water quality and toxic algal blooms have resulted in fish kills, manatee and dolphin die-offs and takeovers by invasive species. But the humans who live here have needs, too: the eastern side of the lagoon is buffered by a stretch of barrier islands that are critical to Florida's economy, tourism and agriculture, as well as for launching NASA missions into space.

As in Florida, many of the world's coastlines are in serious trouble as a result of population growth and the pollution it produces. Moreover, the effects of climate change are accelerating both environmental and economic decline. Given what is at risk, scientists like us—a biologist and a chemist at the University of Central Florida—feel an urgent need to do research that can inform policy that will increase the resiliency and sustainability of coastal communities. How can our research best help balance environmental and social needs within the confines of our political and economic systems? This is the level of complexity that scientists must enter into instead of shying away from.

Although new technologies will surely play a role in tackling issues such as climate change, rising seas and coastal flooding, we cannot rely on innovation alone. Technology generally does not take into consideration the complex interactions between people and the environment. That is why coming up with solutions will require scientists to engage in an interdisciplinary team approach—something that is common in the business world but is relatively rare in universities.

Universities are a tremendous source of intellectual power, of course. But students and faculty are typically organized within departments, or academic silos. Scientists are trained in the tools and language of their respective disciplines and learn to communicate their findings to one another using specific jargon.

When the goal of research is a fundamental understanding of a physical or biological system within a niche community, this setup makes a lot of sense. But when the problem the research is trying to solve extends beyond a closed system and includes its effects on society, silos create a variety of barriers. They can limit creativity, flexibility and nimbleness and actually discourage scientists from working across disciplines. As professors, we tend to train our students in our own image, inadvertently producing specialists who have difficulty communicating with the scientist in the next building—let alone with the broader public. This makes research silos ineffective at responding to developing issues in policy and planning, such as how coastal communities and ecosystems worldwide will adapt to rising seas.

SCIENCE FOR THE BIGGER PICTURE

AS SCIENTISTS WHO LIVE and work in Florida, we realized that we needed to play a bigger role in helping our state—and country—make evidence-based choices when it comes to vulnerable coastlines. We wanted to make a more comprehensive assessment of both natural and human-related impacts to the health, restoration and sustainability of our coastal systems and to conduct long-term, integrated research.

At first, we focused on expanding research capacity in our biology, chemistry and engineering programs because each already had a strong coastal research presence. Then, our university announced a Faculty Cluster Initiative, with a goal of developing interdisciplinary academic teams focused on solving tomorrow's most challenging societal problems. While putting together our proposal, we discovered that there were already 35 faculty members on the Orlando campus who studied coastal issues. They belonged to 12 departments in seven colleges, and many of them had never even met. It became clear that simply working on the same campus was insufficient for collaboration.

So we set out to build a team of people from a wide mix of backgrounds who would work in close proximity to one another on a daily basis. These core members would also serve as a link to the disciplinary strengths of their tenure home departments. Initially, finding experts who truly wanted to embrace the team aspect was more difficult than we thought. Although the notion of interdisciplinary research is not new, it has not always been encouraged in academia. Some faculty who go in that direction still worry about whether it will threaten their recognition when applying for grants, seeking promotions or submitting papers to high-impact journals. We are not suggesting that traditional academic departments should be disbanded. On the contrary, they give the required depth to the research, whereas the interdisciplinary team gives breadth to the overall effort.

Our cluster proposal was a success, and this past January the National Center for Integrated Coastal Research (UCF Coastal) was born. Our goal is to guide more effective economic development, environmental stewardship, hazard-mitigation planning and public policy for coastal communities. To better integrate science with societal needs, we have brought together biologists, chemists, engineers and biomedical researchers with anthropologists, sociologists, political scientists, planners, emergency managers and economists. It seems that the most creative perspectives on old problems have arisen when people with different training and life experiences are talking through issues over cups of coffee. After all, "interdisciplinary" must mean more than just different flavors of STEM. In academia, tackling the effects of climate change demands more rigorous inclusion of the social sciences—an area that has been frequently overlooked.

> "Interdisciplinary" must mean more than just different flavors of STEM. In academia, tackling the effects of climate change demands more rigorous inclusion of the social sciences.

The National Science Foundation, as well as other groups, has recently required that all research proposals incorporate a social sciences component, as an attempt to assess the broader implications of projects. Unfortunately, in many cases, simply adding a social scientist to a proposal is done only to check a box rather than to make a true commitment to allowing the discipline to inform a project. Instead social, economic and policy needs must be considered at the outset of research design, not as an afterthought. Otherwise our work might fail at the implementation stage, which means we are not being as effective as we could be in solving real-world problems. As a result, the public might become skeptical of how much scientists can contribute toward solutions.

CONNECTING WITH THE PUBLIC

THE REALITY is that communicating research findings to the public is an increasingly critical responsibility of scientists. Doing so has a measurable effect on how politicians prioritize policy, funding and regulations. UCF Coastal is being born into a world where science is not always respected—sometimes it is even portrayed as the enemy. There has been a significant erosion of trust in science over recent years, and we must work more deliberately to regain it. The public, we have found, wants to see quality academic research that is grounded in the societal challenges we are facing. That is why we are melding pure academic research with applied research to focus on issues that are immediate—helping a town or business recovering from Hurricane Irma, for example—as well as long term, such as directly advising a community how to build resiliency as flooding becomes more frequent.

As scientists, we cannot expect to explain the implications of our research to the wider public if we cannot first understand one another. A benefit of regularly working side by side is that we are crafting a common language, reconciling the radically different meanings that the same words can have to a variety of specialists. Finally, we are learning to speak to one another with more clarity and understand more explicitly how our niches fit into the bigger picture. We are also more aware of culture and industry as driving forces in shaping consensus and policy. Rather than handing city planners a stack of research papers and walking away, UCF Coastal sees itself as a collaborator that listens instead of just lecturing.

This style of academic mission is not only relevant to issues around climate change. It relates to every aspect of modern society, including genetic engineering, automation, artificial intelligence, and so on. The launch of UCF Coastal has garnered positive attention from industry, government agencies, local communities and academics. We think that is because people do want to come together to solve problems, but they need a better mechanism for doing so. We hope to be that conduit while inspiring other academic institutions to do the same.

After all, we have heard for years to "think globally, act locally," and that "all politics is local." Florida's Indian River Lagoon will be restored only if there is engagement among residents, local industries, academics, government agencies and nonprofit organizations. As scientists, it is our responsibility to help everyone involved understand that problems that took decades to create will take decades to fix. We need to present the most helpful solutions while explaining the intricacies of the tradeoffs for each one. Doing so is only possible if we see ourselves as part of an interdisciplinary, whole-community approach. By listening and responding to fears and concerns, we can make a stronger case for why scientifically driven decisions will be more effective in the long run.

MORE TO EXPLORE

Assessing Scientists for Hiring, Promotion, and Tenure. David Moher et al. in *PLOS Biology,* Vol. 16, No. 3, Article No. e2004089; March 29, 2018.

Sexual Harassment of Women: Climate, Culture, and Consequences in Academic Sciences, Engineering, and Medicine. National Academies of Sciences, Engineering, and Medicine; 2018.

Meta-Research Innovation Center at Stanford (METRICS): **http://metrics.stanford.edu**

FROM OUR ARCHIVES

The Roots of Science Denial. Katharine Hayhoe, as told to Jen Schwartz; State of the World's Science, October 2017.

scientificamerican.com/magazine/sa

SPIKY PROTEIN COAT of the rabies virus (*shown magnified roughly a million times*) enables it to pass from neuron to neuron.

NEUROSCIENCE

RABIES ON THE BRAIN

Using engineered forms of the rabies virus, neuroscientists can map brain circuits with unprecedented precision

By Andrew J. Murray

Andrew J. Murray is a neuroscientist at the Sainsbury Wellcome Center for Neural Circuits and Behavior in London. His group studies how brain circuits generate movement.

LATE ONE MOONLIT NIGHT, three fictional revelers on an English moor were transfixed by a horrific sight: "a foul thing, a great, black beast, shaped like a hound, yet larger than any hound that ever mortal eye has rested upon. And even as they looked the thing tore the throat out of Hugo Baskerville, on which, as it turned its blazing eyes and dripping jaws upon them, the three shrieked with fear and rode for dear life." Historians of medicine have traced the terror that the The Hound of the Baskervilles *evoked in Arthur Conan Doyle's fans to the profound impact of rabies on contemporary British consciousness. With an ability to turn the most placid of pets into frothing, raging beasts and an almost 100 percent mortality rate, the rabies virus was one of the most feared scourges in human history.*

As early as 1804 experiments by German physician Georg Gottfried Zinke indicated that the virus occurs in high concentrations in the saliva of an infected animal. The germ also acts to enhance the production of saliva while increasing the amount of it present in the mouth—explaining why rabid dogs drool. Louis Pasteur went on to demonstrate in the 1880s that the brain, too, is infested with the virus. None of this is an accident. Two centuries of research have now established that the rabies virus combines a propensity to be transferred from the saliva-soaked jaws of an infected animal with a diabolical ability to drive it into a frenzy of aggressive biting. By a feat of evolution, the virus manipulates the host's brain to ensure its own efficient transmission.

Rabies still kills more than 59,000 people annually. Thanks to vaccinations and the quarantine of infected animals, however, it no longer evokes terror in the developed world. Rather neuroscientists are turning the malign germ to the advantage of humankind. The rabies virus is adept at making its way from the site of the bite to the brain by jumping stealthily from neuron to neuron—thereby evading detection by the immune system. A number of researchers, including those in my group at the Sainsbury Wellcome Center for Neural Circuits and Behavior in London, have now harnessed and refined this ability to visualize the connections between neurons.

The human brain consists of billions of neurons, each connected to thousands of others; mapping this tangled web of wires is essential for understanding how it generates our emotions and behaviors. Using engineered varieties of the rabies virus, we can now observe what kinds of inputs a particular type of neuron receives, how electrical signals move from the eye to the brain and what types of neurons control posture to keep us from falling over. Although the field is still in its infancy, in the future such information could help us understand, and perhaps find remedies for, neurological disorders such as Parkinson's disease.

FROM BITE TO BRAIN

TO BEGIN WITH, the bite injects virions, or virus particles, into muscle tissue. A bullet-shaped capsule containing a single strand of RNA and proteins, the rabies virion is coated with a spiky protein, called a glycoprotein. This coat tricks motor neurons that send projections to the assault site into bringing the virus inside. Motor neurons emit chemicals that cause muscles to contract, and they are linked by a long chain of other neurons to the victim's brain—the virus's ultimate destination.

To be precise, the glycoprotein binds to a receptor on a synaptic terminal of the neuron: a point where it transmits signals to a neighboring neuron. Like a door through which one only exits the secure area of an airport—but not enters—the synaptic terminal guards a one-way passage—a synapse—between the neurons. By convention, the "downstream" direction of the synapse is the flow of signals from one neuron to the next, all the way from the brain to the muscles. The rabies virus travels upstream, however, because it has to get to the brain. As such, it fools the receptor to enter a motor neuron through the exit gate.

Viruses are adept at using their host's cells for their own purposes, but few can beat rabies at the task. Once inside, the intruder throws off its glycoprotein disguise, and its RNA gets to work,

IN BRIEF

The rabies virus is adapted to jumping from one neuron to another as it makes its way from the site of a bite to an animal's brain.

Virologists and neuroscientists have harnessed this capability to identify the neurons that send signals to the particular neurons they are studying.

The technology involves engineering the rabies virus so that it glows, infects only the neurons of interest and can jump once across a connection.

PAGE 68: CHRIS BJORNBERG *Science Source* using the cell's materials and metabolism to produce copies of itself, as well as of all its characteristic proteins. These components then reassemble to create daughter virions. Whereas many virus species replicate so rapidly that they force the infected cell to burst open, releasing the virions into the space between the cells, the rabies virus strictly regulates its reproduction—producing just enough daughters to keep moving on. That way, it refrains from causing so much damage that it alerts the immune system. Instead it leaves the host cell intact and crosses a synapse to a new upstream neuron. That sneakiness is one reason the disease has such a long, symptomless incubation period, typically one to three months in humans.

Having thus jumped to a new neuron, the virion starts the entire process again: undressing and copying itself and reassembling daughters that move into the next upstream neuron. In this way, the rabies virus picks a path through the nervous system, creeping from the motor neuron it first encountered in the muscle tissue, through the spinal cord and into the brain.

By the early 2000s several research groups, including those of Gabriella Ugolini, now at the Paris-Saclay Institute of Neuroscience, and Peter Strick, now at the University of Pittsburgh, were pursuing the use of rabies as a tracer for neuronal circuits. Deciphering the route that the virus took from the muscle to the brain was a challenge, however. As a neuroscientist looking at a snapshot of neurons that had been infected with the virus, how could you distinguish between the first jump of the invader from one neuron to the next, the second jump, and so on?

The researchers initially solved this problem by euthanizing laboratory animals shortly after infection, thereby allowing the virus to spread across only one or two synapses. This approach uncovered some of the major pathways in the brain that contribute to motor control. But it had its drawbacks. Not all connections between neurons are equal. A synapse may be strong (or weak), making it more (or less) likely that a signal moving across it will prompt the target neuron to fire in response. Another might be located close to the cell body instead of far away at the end of a projection. And some neurons make a single link with a downstream neuron, whereas others may make hundreds. This heterogeneity means that the virus takes varying lengths of time to travel from one neuron to the next, adding a layer of uncertainty. What if the virus moves through two or three strong synapses before it passes through a weak one?

VIRAL ENGINEERING

TO GET AROUND this problem, scientists needed to rejigger the rabies virus. Molecular biologists have developed the amazing ability to manipulate DNA: swapping out genes has become as routine for them as making coffee in the lab kitchen. The wild rabies virus has no DNA to manipulate, however, only RNA. The advent of reverse genetics, which flips the normal genetic cycle by making RNA from DNA, got around that hurdle. In 1994 Matthias Schnell and Karl-Klaus Conzelmann, both then at the Federal Research Center for Virus Diseases of Animals in Tübingen, Germany, produced a functional rabies virus in the lab from cloned DNA alone. They even altered the rabies genome: the RNA string that encodes its characteristic properties.

The ability to manipulate the genome swiftly led to a greater understanding of how the different rabies genes contribute to the virus's diverse skills. Only one gene was essential to its ability to move between neurons, it turned out: the one that coded for glycoprotein. A rabies virus that had the glycoprotein gene removed from its genome could infect a cell, but once inside it was stuck there. This would be the discovery that thrust the virus into mainstream neuroscience.

In 2007 a collaboration between neuroscientists Ian Wickersham and Edward Callaway, both then at the Salk Institute for Biological Studies in La Jolla, Calif., and virologists Conzelmann and Stefan Finke of the Friedrich Loeffler Institute in Germany resulted in an ingenious system to map neuronal circuits. The first step in their scheme was to swap the glycoprotein gene in the rabies genome with one that coded for a fluorescent protein. The engineered virion could not manufacture glycoproteins; instead its RNA made copies of the fluorescent protein (along with all the other rabies proteins)—so the infected cell shone with a bright color of the experimenters' choosing.

The second step was to provide glycoprotein in the targeted neuron via some other genetic mechanism. That way, the daughter virions could don glycoprotein coats and jump once—but no more. To that end, the scientists harnessed a very simple type of virus, called an adeno-associated virus (AAV) because it is often found along with much larger viruses called adenoviruses. AAVs contain a tiny amount of DNA. The Salk researchers inserted a gene for making the rabies glycoprotein into that DNA. The rabies virion could harness the glycoprotein the gene manufactured to jump across a single synapse. It could not, however, take the glycoprotein gene with it because it was a segment of DNA, not of RNA. So when the virion had jumped into the next cell, it was stuck again. At that point, a glance at the infected animal's brain revealed populations of glowing cells across the nervous system that were directly connected to any neuron researchers wanted to target.

There remained one problem, however. Injection of the rabies virus into the brain resulted in the direct infection of any neuron that sent a projection into the injection site. Without a way to restrict the initial infection of the rabies virus to particular neurons, scientists could not differentiate between neurons that were infected directly by the injected virus and those that were infected after the virus had moved across a synapse. The solution would come from another area of virology: viruses that specifically affect birds.

In the wild, entire classes of viruses can be found that infect only certain groups of animals. For example, the avian sarcoma leukosis virus (ASLV) usually leads to cancer in chickens but cannot normally infect mammalian cells. Like rabies, this virus has a glycoprotein envelope, which comes in a variety of configurations. Different ASLV glycoproteins are known as Env (for envelope), followed by a label for the particular form. Each subtype binds to a specific receptor. So, for example, EnvA binds to a receptor called TVA (for avian *t*umor receptor *v*irus *A*). If a cell does not possess the TVA receptor, it cannot be infected with an EnvA-coated virus. This selective interaction enables researchers to restrict the initial infection of rabies virus to one type of neuron.

By introducing the gene for EnvA glycoprotein in a rabies-infested cell culture (a process known as pseudotyping), Wickersham, Callaway and their colleagues replaced the native glycoprotein coat on the rabies virus with the EnvA glycoprotein from the avian virus. Thus altered, the rabies virus could not deceive any mammalian cells into letting it in. By endowing the neuron of interest, typically in a mouse brain, with the TVA receptor, neuroscientists could be assured that the rabies virus would infect only this cell.

Using Rabies to Track Brain Circuits

The rabies virus makes its way from the bite to the brain by jumping from one neuron to the next. Virologists and neuroscientists have harnessed and modified this ability to see how neurons connect into complex circuits.

NORMAL RABIES PATHOLOGY

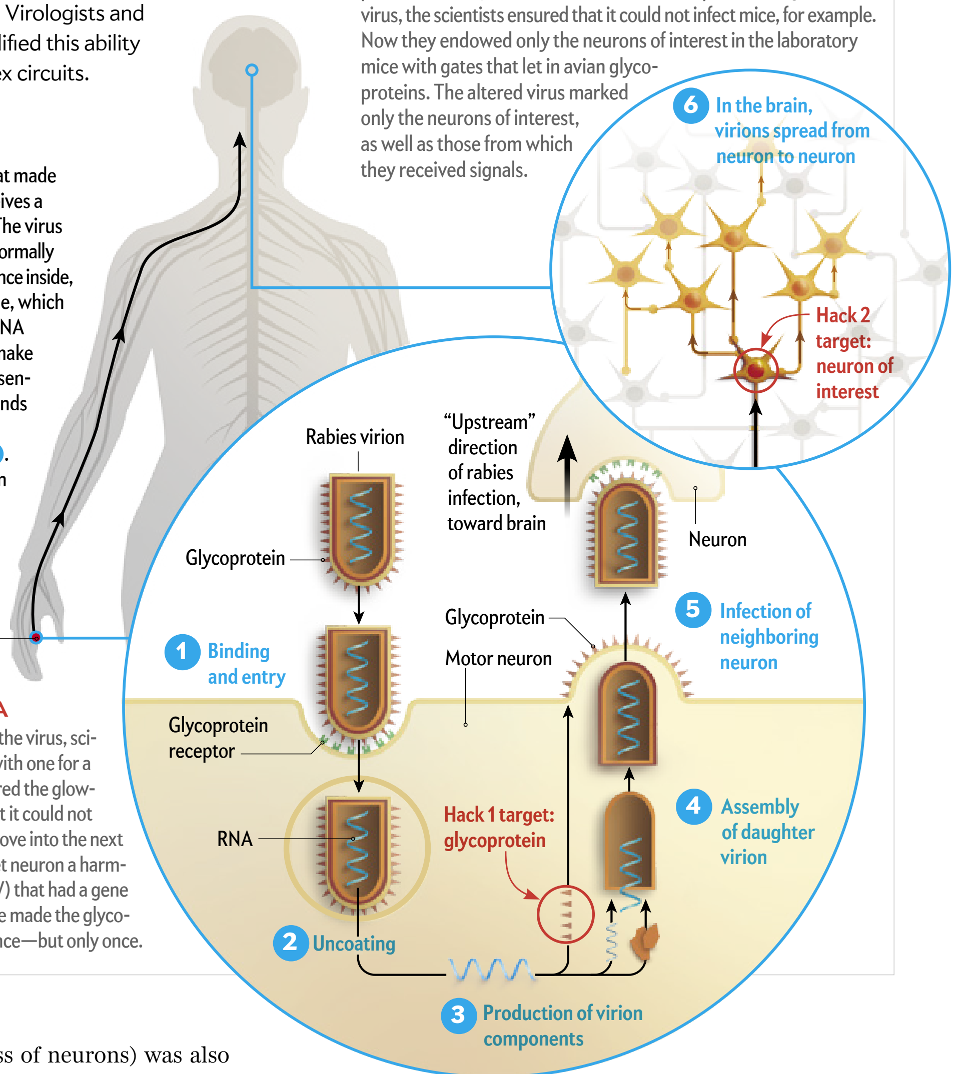
The rabies virion, or virus particle, has a coat made of glycoprotein (a type of protein) that deceives a nearby motor neuron into letting it in (1). The virus enters at a synaptic terminal, or gate, that is normally used to send information to other neurons. Once inside, the virus sheds its coat to release its genome, which is made of RNA rather than DNA (2). The RNA uses the neuron's metabolic machinery to make multiple copies of itself and of the virus's essential proteins (3). The proteins and RNA strands reassemble into daughter virions (4) that move upstream into connected neurons (5). In this manner, the virus moves from neuron to neuron on its way to the brain, where it continues to propagate (6).

HACK 1: ENGINEERING RABIES RNA

To ensure that they could follow the exact route of the virus, scientists replaced the glycoprotein gene in its RNA with one for a fluorescent protein. The modified RNA manufactured the glowing protein, so that the infected neuron glowed, but it could not make the glycoprotein. Thus, the virus could not move into the next neuron. Next, the researchers added into the target neuron a harmless virus (called an adeno-associated virus, or AAV) that had a gene for rabies glycoprotein added to its DNA. That gene made the glycoprotein, which the virions could harness to jump once—but only once.

HACK 2: ALTERING THE GLYCOPROTEIN COAT

To restrict the rabies infection to the neurons of interest, experimenters used the fact that glycoprotein comes in various types. The glycoprotein coats worn by certain viruses that target birds cannot normally enter mammalian cells. So by replacing the usual glycoprotein covering of the rabies virus with that possessed by an avian virus, the scientists ensured that it could not infect mice, for example. Now they endowed only the neurons of interest in the laboratory mice with gates that let in avian glycoproteins. The altered virus marked only the neurons of interest, as well as those from which they received signals.



The target neuron (in practice, a class of neurons) was also supplied with an AAV containing the gene for rabies glycoprotein. Once inside, the rabies virus shed its chicken costume, picked up its normal cloak and jumped into upstream neurons. By engineering the rabies virus to infect—and hop only once from—a well-defined group of "starter" neurons, researchers could now get a clear image of how the brain was wired.

TUNING RABIES

THE SIMPLICITY AND ELEGANCE of the delta-G rabies system (as its inventors called it because of the altered glycoprotein) took the neuroscience community by storm. Using it, researchers could see right away what kinds of neurons send signals to the neurons of interest. Like all new technologies, however, the scheme had its imperfections. Sometimes the number of connections labeled were rather small—on the order of 10 per starter neuron.

Around 2015 Thomas Reardon, Thomas Jessell, Attila Losonczy and I, all then at Columbia University, were using the delta-G system to understand the neural circuits that guided motor commands. Finding relatively low numbers of connections to motor neurons in the spinal cord or the brain, we suspected we were getting an incomplete picture of the circuitry. Another issue was neurotoxicity. Once the virus was in a cell, it would start to break down and die within a couple of weeks. If the virus itself was causing individual neurons to alter their behavior, interpreting any observations could be problematic.

Schnell and Christoph Wirblich, both at Thomas Jefferson University, had done pioneering work on rabies virus biology, so we went to them for help. They knew right away that our problems stemmed from the strain of virus that we were using. It had originally been developed for use in a rabies vaccine. Vaccines incorporate special strains of the germ that humans have selected to reproduce unusually rapidly so that the multitudinous daughter virions explode out of the infected cells and alert the immune sys-

Illustration by Kelly Murphy

tem before it is too late. That indicated a way to refine our research tool. Because we were using mice in our studies, our virologist collaborators suggested that we instead try a strain that had been tuned over many years to infect mouse neurons.

The parent virus of this strain had originally been isolated in the wild and then "fixed" in the lab by being repeatedly passed through the brains of mice or through cell lines. It had thereby evolved to be a specialist at targeting the mouse nervous system. After assembling a neuronal tracing mechanism based on this mouse-specific strain, we found that it labeled many more connections than we had previously seen. Moreover, being an expert at evading the mouse immune system, it made relatively small amounts of each protein. As such, it placed less strain on the host cell's machinery and allowed neurons to remain relatively healthy.

We further altered our tracing system to replace the gene for the fluorescent protein in the rabies virus with one for a light-sensitive protein, called channelrhodopsin (ChR), originally found in green algae. When activated by blue light, this remarkable molecule opened a channel that allowed positively charged ions to flow into the target neuron, prompting it to emit an electrical signal. (The infected cell continued to glow, however, because we used a version of ChR that included a fluorescent protein.) With this fine-tuned rabies virus system, we could watch entire neuronal circuits fire during certain actions of the mouse or switch them on or off—for up to a month after the virus had infected a neuron. That gave us ample time to conduct many of the tests we needed to understand how specific circuits generate behavior.

WIRING DIAGRAM

USING DIFFERENT VERSIONS of the delta-G rabies system, neuroscientists have probed many different circuits in the nervous system to understand how they contribute to the perceptions and behaviors of animals. Take, for instance, the visual system. When light enters the eye, neurons at the back of the retina, called retinal ganglion cells, transmit signals to the brain. Neuroscientists traditionally believed that this information travels to intermediate locations in the brain, ultimately ending up in the cerebral cortex—the celebrated gray matter—where it is processed. Botond Roska's group at the Friedrich Miescher Institute for Biomedical Research in Switzerland used the rabies system to trace the inputs from the retinal ganglion cells to the lateral geniculate nucleus (LGN), an area of the brain that was regarded as just another relay to the cortex.

The researchers demonstrated that the LGN contained three different types of neurons, each likely processing visual information differently. Indeed, less than a third of the neurons served as a relay, providing a direct line from the retina to the cortex. But roughly another third received combinations of different inputs from one eye; the remaining neurons (about 40 percent) got signals from both eyes. Thus, although the LGN lies at an early stage of the visual circuit, most of its neurons integrate information from multiple sources. The finding will likely illuminate the process by which the brain interprets information from the eyes.

At Columbia, my co-workers and I investigated the neurons in the lateral vestibular nucleus (LVN), a brain region that tries to prevent us from falling over. Imagine being on a moving subway train that stops unexpectedly. Before you have had time to think, you shift your feet to compensate, stiffen your legs and perhaps grab the nearest pole. How does the brain activate the right groups of muscles so swiftly in a variety of similar situations?

We found that the LVN of mice contains two anatomically distinct types of neurons, each having different downstream connections to parts of the nervous system. One group switches on very quickly after your brain senses your body is unstable; these neurons act to extend the limbs to widen the base of support. Later, a second set of LVN neurons become active. These serve to strengthen and stabilize the joints in the same limb, enabling the body to be pushed back to its original position. We could activate these neurons simply by switching on a blue light, delivered to the LVN by a fiber-optic cable. When the light came on, the mice adjusted the positions of their limbs, as if to stop themselves from falling over—even when they were not off-balance.

Nao Uchida's lab at Harvard University investigated a third significant question: What are the functions of neurons that release dopamine? Such "dopaminergic" neurons in two regions of the brain, the substantia nigra pars compacta (SNc) and the ventral tegmental area (VTA), have long been known to respond to rewards. They would become very excited when a test animal got a treat or when a sensory stimulus predicted that it was about to come. (Think of eating a candy bar, compared with hearing the rustling of its wrapper.) To understand what types of information the neurons were receiving, scientists needed to know how they were connected to other brain circuits. Using the delta-G system, the Harvard team found that dopaminergic neurons in the SNc received information about the relevance of a stimulus: Is this sound of a candy wrapper going to get me a piece of chocolate? In contrast, the VTA received information on the quality of the reward: How good is this candy?

As it happens, dopaminergic neurons in the SNc degenerate in Parkinson's. Intriguingly, Uchida and his colleagues also discovered that major inputs into such neurons in the SNc come from the subthalamic nucleus, a small, lens-shaped region of the brain that, along with similar nuclei, is involved in controlling movement. Exciting the subthalamic nucleus by means of an inserted electrode, in a technique known as deep-brain stimulation, is often effective at relieving symptoms of Parkinson's. Surmising that the inputs they had discovered explained why such stimulation works, the neuroscientists reasoned that targeting other brain regions, which they had identified as also sending inputs to the SNc, might aid some Parkinson's patients.

The combination of natural evolution and targeted engineering has thus given neuroscientists a remarkably powerful tool. There is still much room for improvement. For example, will it be possible to engineer viruses that move downstream, labeling a neuron's outputs instead of its inputs? Can we make a virus that labels only active connections between neurons, lighting up the circuits that are involved in distinct behaviors? The time has come for a virus that has manipulated and terrorized humans for millennia to be manipulated to serve us. SA

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NATURAL DISASTERS

THIS WAY OUT

Evacuating an entire city ahead of a threatening storm is all but impossible. New risk maps highlight who really needs to leave

By Leonardo Dueñas-Osorio, Devika Subramanian and Robert M. Stein

STORM STRUGGLES: When Hurricane Harvey aimed at Houston in 2017, officials had to weigh the dangers of inundation against the perils of mass exodus.


Leonardo Dueñas-Osorio is a civil and environmental engineer at Rice University.


Devika Subramanian is a computer scientist at Rice.


Robert M. Stein is a political scientist at Rice.

WE DID NOT INTEND TO HURT ANYONE. OUR GOAL HAD BEEN TO HELP our neighbors in the Houston area get out of danger. Yet in 2015 the phone started ringing, and Internet messages started piling up, saying we were making safety worse. "You are doing a disservice," said one public official from a district on Houston's northern edge. A meteorologist chastised us: "How come you are telling people they are at low risk for flooding when there is flooding all around them?"

The messages were about our Web-based map, the Storm Risk Calculator (SRC), which we developed and operated for the city. We had designed it to tell residents which of them should flee in the face of an oncoming hurricane because their homes could be destroyed and who could stay because their house was likely to remain safe. The dangers were real: this region had been pummeled by Hurricanes Rita and Ike several years earlier. But clearly something about our map had gone wrong.

When cities near the coast like Houston face severe storms, evacuations seem the obvious way to protect people. But moving millions of people carries its own dangers. When Rita took aim at our area in 2005, officials told everyone to leave. Giant traffic jams turned Interstates 45 and 10 and U.S. Route 59 into parking lots as people at low risk fled, blocking escape routes for individuals who needed them most—residents directly in the path of high winds, heavy rain and storm surge. A few died on the road in the tremendous heat. A bus evacuating residents from a nursing home caught fire, igniting an oxygen tank and killing 23 onboard. So when Hurricane Harvey bore down on Houston last August, Mayor Sylvester Turner refused to evacuate. "You literally cannot put 6.5 million people on the road," he said at the time. "If you think the situation right now is bad, you give an order to evacuate, you are creating a nightmare."

In the years after Rita and Ike, the three of us—an engineer, a computer scientist and a political scientist focused on public safety—decided to help Houston fix this nightmarish situation. We built our interactive SRC map to show safe and unsafe regions in the face of hurricane-force winds and storm surge. But we learned, after the complaints started piling up, that our map was focused on the wrong things. Houstonians and people in the surrounding area, Harris County, worry about major floods from heavy rainstorms, not just hurricanes, because the region gets a lot more of the former. People also wanted risk information on a much finer scale than our map provided.

This situation pushed us into a major research project to understand people's views of risk and to develop new sources

PRECEDING PAGES: MARCUS YAM *Getty Images*

IN BRIEF

In big cities, getting out of a storm path has provoked mass panic and clogged escape routes, with deadly results.

The trouble has been that warnings are too general, lumping together people at high and low risk for things like hurricane damage and flooding.

A new type of risk map, being tested in flood-prone Houston, uses fine-scale data to pinpoint high-risk homes and reassure those who can safely stay.

NOT JUST A RAINSTORM: In Houston, it does not take a hurricane to flood neighborhoods. Heavy downpours frequently imperil people and homes, as this storm did in 2016.

DAVID J. PHILLIP AP Photo

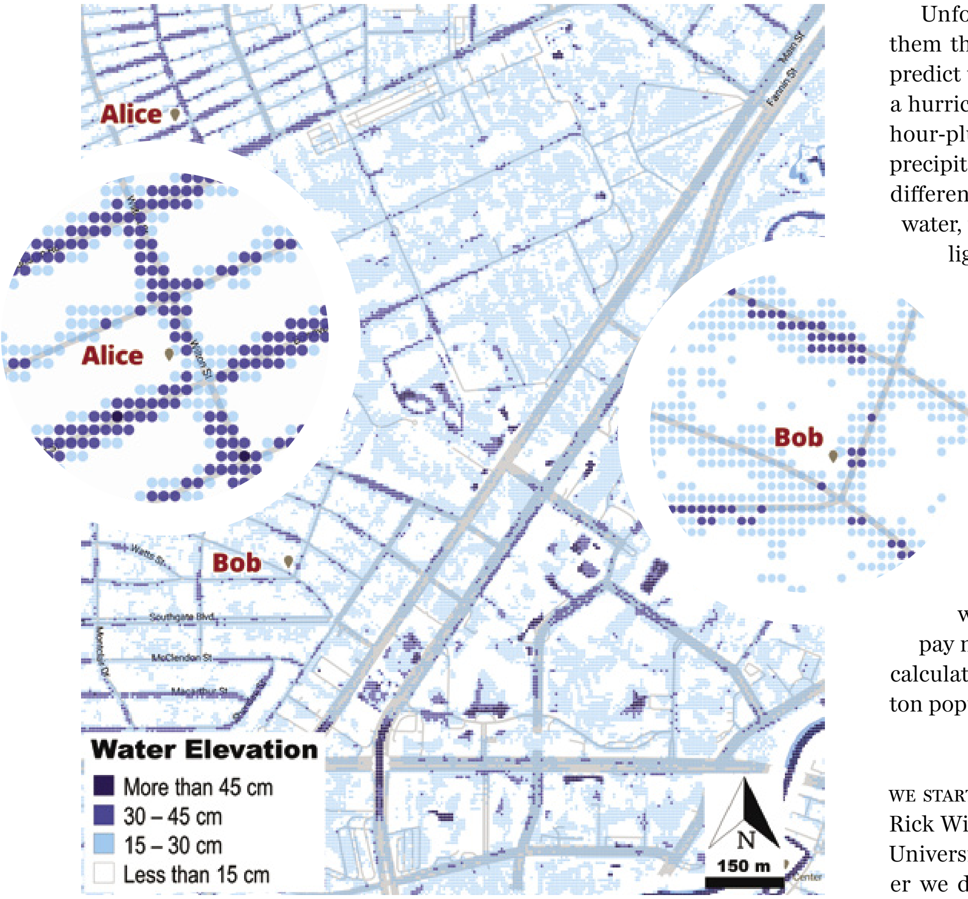
of data. As a result, we have rebuilt our risk map from the ground up, using more refined data about the dangers that truly affect homes and residents in our area. The new risk map, which will start live testing next year, integrates better data about more types of storms with cutting-edge artificial-intelligence technology, all to show people the risks to individual city blocks, as well as the best routes out. If the model works as we hope it will, it can be used by emergency planners to deploy resources in ways that have never before been available and to save more lives.

CALCULATED RISKS

WHEN WE STARTED the SRC project, we wanted to provide estimates of the main risks from hurricanes, including damage from storm surge, wind, rising water in bayous and power outages. We used data on real-time wind fields from the National Oceanic and Atmospheric Administration, along with rainfall levels reported by the Harris County's Flood Warning System and home characteristics from the Harris County Appraisal District, such as the date of construction—which can reveal how strongly the roof is fastened to the walls. The resulting model predicted risk of house damage or power outage in different areas, in one-kilometer squares. When we tested it against various simulated hurricanes, as well as the actual damage from Hurricane Ike, the accuracy level in a typical square was better than 70 percent. Previous evacuation maps would give only a prediction based on things such as storm surges across an entire zip code, which can cover hundreds of square kilometers. So the new chart was a big improvement.

To picture the SRC in operation, imagine a hurricane in the Gulf of Mexico destined to hit Houston in a couple of days. One resident, Alice, simply needed to type in her address, and she would see a map. A color-coded, low-medium-high scale would indicate damage chances from wind, storm surge, bayou flooding and power outages. Her risks for wind damage would be fairly high. Alice's two-story home, built in the 1960s, faced an open park in front of a bayou, and winds do not slow down in open areas. And the bayou would fill with wind-driven rain and raise her chances of flooding.

Another user, Bob, with a house about two kilometers away, would have a lower risk. Bob's home, built in the 1990s, is just one story high and surrounded by trees. The lower house would catch less wind. The trees also would slow the winds, reducing their impact, and his more modern roof-to-wall connections



DANGER ZONES: This map of a two-square-kilometer swath of Houston, from the computer program HARVEY, predicts effects of a 20-centimeter rainstorm. One resident, Alice, would be flooded while another, Bob, would be at less risk.

would make his structure stronger. (Snapping tree branches, however, could come down on power lines and make electrical outages very likely.) Bob was also farther away from the bayou, lowering chances of flood damage. Better informed of their risks, Alice could decide to leave, while Bob could choose to stay, even though they were facing exactly the same storm.

The calculator was popular right after the city announced it was up and running in June 2012. About 40,000 people used it in the days immediately after the launch. Usage soon leveled off to approximately 1,000 viewers a month and stayed that way for the next several years. But there was something odd. Houston did not have any hurricanes from the time we launched through 2016, yet map traffic spiked during large rainfall events. A heavy downpour can cause big problems. The city sprawls, and rapid urban and suburban growth has replaced water-absorbing meadows and stream channels with miles of concrete, which shunts water into neighborhoods and floods houses. In 2015 we had the Memorial Day flood and the Halloween flood. In 2016 we had the Tax Day flood. Twenty to 30 centimeters of rain—eight to 12 inches—fell during events like these; some bayous could not channel away all the water and topped their banks, and homes were ruined. When local forecasters started talking about several hours of heavy rain, people turned to our map.

Unfortunately, the map was not providing them the right information. It was designed to predict the effects of Gulf water driven inland by a hurricane and damage from 120-kilometer-per-hour-plus winds. Several dozen centimeters of precipitation dropping straight from the sky had different effects. Inland areas could get a lot of water, for example, but our map would not highlight that as a risk. That is when we started to get the complaining phone calls.

The last straw came in 2016, when the cloud server that held our SRC program was hacked. Hackers cut off our access and demanded money to give it back. It was a classic ransomware move. We had had enough. The more often the site appeared to give out misinformation, the greater the chance that people would lose trust in the program. It was time to shut the map down. We would pay no blackmail. But we would rebuild a risk calculator based on the actual needs of the Houston population, not on hurricane season alone.

REDRAWING THE MAP

WE STARTED BY REACHING OUT to a close colleague, Rick Wilson, a behavioral social scientist at Rice University, who studies decision making. Together we designed a series of online experiments, using risk maps, in which hundreds of Houstonians were randomly assigned to various levels of data resolution and risk type. We focused on the time spent searching a map: more time indicated citizens' interest in storm risks and their willingness to take action to prepare. Although big hurricanes—say, category four—got the most notice, attention disappeared if the geographical data on storm effects were not local. People were not interested in maps divided into areas that were a kilometer wide or partitioned by zip code. But when the map showed data on almost every block, hundreds of users sought more information. We also learned that, particularly in inland areas, projected rain amounts got more interest than projected storm surge levels. Serious rain events affect people's mobility, productivity and safety.

These behavioral experiments showed that individuals pay the most attention to risks they perceive as most relevant to their own situation. This is obvious to us in hindsight, but think of how it contrasts with the way most storm information is handed out today—official blanket statements for rare events covering areas of many hundreds of square kilometers, such as entire counties and zip codes.

With our new focus on local events, we began to build a system around rainfall runoff and accumulation. We call it the Hurricane and Rain Vectorized Exposure Yielder, conveniently abbreviated to HARVEY. Our computer model HARVEY has a much finer geographical terrain grid than our earlier map, using cells that are only several square meters, instead of square kilometers. A single street can have many of these new squares, and

HESAM TALEBIYAN, JAYANT PATIL AND KYLE SHEPHERD *Rice University* the total for the city is more than 100 million of them. This configuration provides much more precise estimates of overland water flows and their depths when it rains intensely.

We used a variety of sources to derive these estimates. We had the history of National Weather Service forecasts and data, of course, but our model also incorporates the locations of calls to Houston's 311 city information service to report local flooding. We can also draw on emergency calls to fire and police departments asking for help. Repeated calls from a particular location indicate recurring trouble spots. Harris County has a network of rain gauges, and we pull data from them. (We are also testing a wireless network of street-level flood sensors.) Our prediction models also include radar data that show how much water is held in the clouds heading for the city and how fast the wind is moving them. Slower winds give the clouds time to dump a great deal of water. That scenario produces a lot of nonhurricane flooding and was behind the inundation created by slow-moving Hurricane Harvey last year.

Our HARVEY system will show users the dangers that affect route choices, the possibility of getting trapped and the likely levels of flooding for homes.

All these data are superimposed on a high-resolution terrain map, derived from the Houston-Galveston Area Council's laser-driven remote-sensing system, which captures minute differences in ground height. The entire thing is integrated by AI programs that use fancy-termed techniques such as ensemble regression models, deep-learning algorithms and high-dimensional vector spaces. But the basic point is they are much more capable of combining different types of data sets than were the engineering models and mathematics we used for our original storm calculator.

We have tested HARVEY by giving it several sets of initial conditions seen prior to storms since 2015 and have asked the program to produce flood estimates for multiple places across the city. The predictions HARVEY has churned out have matched actual field observations of these storms well. The program does best with heavy downpours, more than five centimeters—two inches—per hour that last several hours, and in spots with poor drainage because of bayou overflows and bay tides. For smaller events, we will be calibrating HARVEY one watershed at a time over multiyear periods, to capture local factors and longer-term effects of climate change.

What would this mean for our worried Houstonians Bob and Alice? Our new map would provide them different levels of risk, with more attention paid to the history of flooding near Alice's house and the height of the land around Bob's. The key difference is that even if Bob and Alice lived two blocks apart, rather than two kilometers, they would be given different risk levels. With the erratic rainfall patterns across the city for any single event, users like Alice and Bob may find very different estimates of street flooding around their homes, their workplaces and the routes in between. Our HARVEY system will show users like them the dangers that affect route choices, the possibility of getting trapped at their locations and the likely levels of flooding for homes during rainfall events. It will help the city government allocate emergency and planning resources in advance, allowing first responders, such as the fire department, to get to people in trouble faster. Storm-mitigation projects can be located in areas that need them most.

Our plan right now is to publically launch a beta version of HARVEY in 2019, designed specifically for residents of the hard-hit Brays Bayou watershed. This waterway crisscrosses a neighborhood called Meyerland, where homeowners have been surprised by flooding multiple times during the past five years. Their residences have been wrecked, rebuilt and wrecked again. On many occasions people have been stuck in these houses, watching the water rise. We hope to give them better and earlier warnings. Our next step will be to expand the system to reach the rest of the city. Our team is entering into a collaborative agreement with the city of Houston, the Kinder Institute for Urban Research, and the Severe Storm Prediction, Education, & Evacuation from Disasters (SSPEED) Center to test and deploy HARVEY in stages toward future city-wide coverage. And if the model works for Houston, it could be adapted to other cities across the world that face similar problems from severe weather.

A changing global climate is going to make rainfall worse in our region, according to conclusions reached by a 2018 Houston severe storm conference organized by the SSPEED center. Storms will stagnate more frequently, dumping more rain as a consequence. Tools such as HARVEY will provide flood estimates at a scale that public officials and private citizens seek as they try to plan for this intensifying chronic rainfall and runoff. Most important, these tools will give people who must live under these clouds the ability to answer, for their own safety and that of others, one urgent question: Should I stay, or should I go? SA

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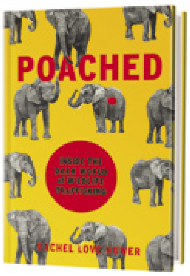
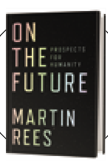


CHARRED REMAINS of an African elephant poached for bushmeat in Chobe National Park, Botswana.

From the swampy wilderness of southern Vietnam, where hunters pursue threatened pangolins, to a bustling wholesale traditional medicine market in Guangzhou, China, where the pinecone-resembling mammal's scales are sold, journalist Nuwer brings the reader along on her globe-trotting mission to understand the complex, thriving world of the illegal wildlife trade. She interviews hunters who capture endangered species, practitioners of Chinese traditional medicine who ingest rhino horn powder for unproved benefits and the conservationists trying to stem the slaughter of dozens of dwindling species. Forces such as entrenched poverty and corruption prevent easy solutions to the wildlife trafficking, especially given the limited resources of local governments and existing reserves. While the accounts can be gut-wrenching, Nuwer finds rays of hope in the park rangers and other conservation experts who are dedicating their lives to saving some of the earth's most majestic creatures. *—Andrea Thompson*

On the Future: Prospects for Humanity

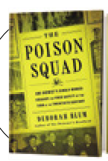
by Martin Rees. Princeton University Press, 2018 ($18.95)



Powerful new technologies—from gene editing to geoengineering—are poised to remake life as we know it. These innovations could prove fruitful or damaging, depending on how we deploy them. Astrophysicist Rees neatly packages his sprawling subject matter into a guidebook for the responsible use of science to build a healthy and equitable future for humanity. He ponders the prospects of long-term palliative care: Should doctors use technology to keep vegetative patients alive indefinitely? And should "objective" artificially intelligent computers recommend surgeries or launch bombs instead of biased humans? Such questions constitute Rees's spirited assessment of technology's role in shaping our future—whether constructive or catastrophic. *—Daniel Ackerman*

The Poison Squad: One Chemist's Single-Minded Crusade for Food Safety at the Turn of the Twentieth Century

by Deborah Blum. Penguin Press, 2018 ($28)



Milk whitened with chalk. Peas made greener with copper. Chemicals added to meat to prolong a pinkish, fresh hue. In the late 1800s U.S. food manufacturers took these liberties, along with dozens more, to trim costs. Journalist Blum chronicles the efforts of one chemist to fight back against these dangerous practices. Her subject, Harvey Washington Wiley, was an outspoken political actor, who sparred with the likes of Theodore Roosevelt in an effort to regulate the industry. Blum draws from her meticulous research to re-create the battle between regulation in the name of consumer protection and production in the name of profits. *—Maya Miller*

Laika's Window: The Legacy of a Soviet Space Dog

by Kurt Caswell. Trinity University Press, 2018 ($24.95)

In 1957 the Soviet Union sent its second satellite into orbit around Earth, this one carrying a dog named Laika. Sputnik 2 made 2,570 revolutions over five months before its fiery reentry in our planet's atmosphere. Laika did not survive her journey—an outcome the space agency anticipated. Writer Caswell profiles the program that trained dozens of such "space dogs" as test subjects for early missions. Plucked from the streets of Moscow, Laika endured extreme gravitational forces, vibration and long periods of isolation. She was the first animal to orbit Earth. The program was a "tipping point" for space exploration, Caswell writes, but Laika's treatment was undeniably cruel. The book is meant as a testament to her experience.

JASON EDWARDS *Getty Images*

Michael Shermer is publisher of *Skeptic* magazine (www.skeptic.com) and a Presidential Fellow at Chapman University. His new book is *Heavens on Earth: The Scientific Search for the Afterlife, Immortality, and Utopia.* Follow him on Twitter @michaelshermer

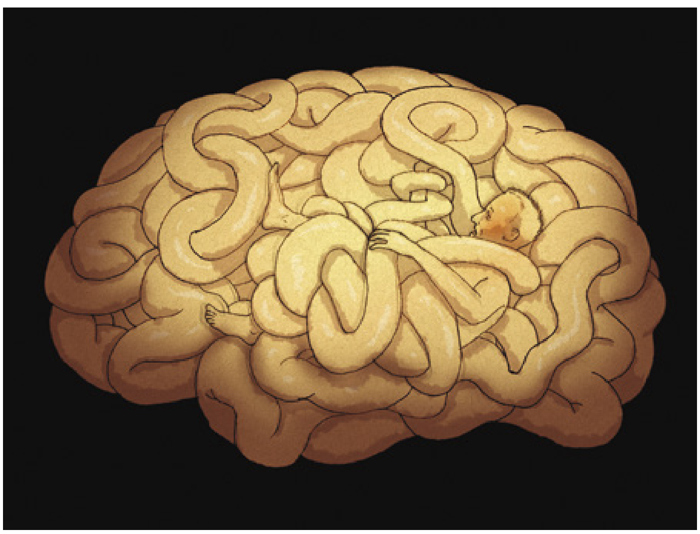
A Mysterious Change of Mind

Why do people die by suicide?

By Michael Shermer

Anthony Bourdain (age 61). Kate Spade (55). Robin Williams (63). Aaron Swartz (26). Junior Seau (43). Alexander McQueen (40). Hunter S. Thompson (67). Kurt Cobain (27). Sylvia Plath (30). Ernest Hemingway (61). Alan Turing (41). Virginia Woolf (59). Vincent van Gogh (37). By the time you finish reading this list of notable people who died by suicide, somewhere in the world another person will have done the same, about one every 40 seconds (around 800,000 a year), making suicide the 10th leading cause of death in the U.S. Why?

According to the prominent psychologist Jesse Bering of the University of Otago in New Zealand, in his authoritative book *Suicidal: Why We Kill Ourselves* (University of Chicago Press, 2018), "the specific issues leading any given person to become suicidal are as different, of course, as their DNA—involving chains of events that one expert calls 'dizzying in their variety.'" Indeed, my short list above includes people with a diversity of ages, professions, personality and gender. Depression is commonly fingered in many suicide cases, yet most people suffering from depression do not kill themselves (only about 5 percent Bering says), and not all suicide victims were depressed. "Around 43 percent of the variability in suicidal behavior among the general population can be explained by genetics," Bering reports, "while the remaining 57 percent is attributable to environmental factors." Having a genetic predisposition for suicidality, coupled with a particular sequence of environmental assaults on one's will to live, leads some people to try to make the pain stop.



In Bering's case, it first came as a closeted gay teenager "in an intolerant small Midwestern town" and later with unemployment at a status apex in his academic career (success can lead to unreasonably high standards for happiness, later crushed by the vicissitudes of life). Yet most oppressed gays and fallen academics don't want to kill themselves. "In the vast majority of cases, people kill themselves because of other people," Bering adduces. "Social problems—especially a hypervigilant concern with what others think or will think of us if only they knew what we perceive to be some unpalatable truth—stoke a deadly fire."

Like most human behavior, suicide is a multicausal act. Teasing out the strongest predictive variables is difficult, particularly because such internal cognitive states may not be accessible even to the person experiencing them. We cannot perceive the neurochemical workings of our brain, so internal processes are typically attributed to external sources. Even those who experience suicidal ideation may not understand why or even if and when ideation might turn into action.

This observation is reinforced by Ralph Lewis, a psychiatrist at the University of Toronto, who works with cancer patients and others facing death, whom I interviewed for my Science Salon podcast about his book *Finding Purpose in a Godless World* (Prometheus Books, 2018). "A lot of people who are clinically depressed will think that the reason they're feeling that way is because of an existential crisis about the meaning of life or that it's because of such and such a relational event that happened," Lewis says. "But that's people's own subjective attribution when in fact they may be depressed for reasons they don't understand." In his clinical practice, for example, he notes, "I've seen many cases where these existential crises practically evaporated under the influence of an antidepressant."

This attributional error, Lewis says, is common: "At a basic level, we all misattribute the causes of our mental states, for example, attributing our irritability to something someone said, when in fact it's because we're hungry, tired." In consulting suicide attempt survivors, Lewis remarks, "They say, 'I don't know what came over me. I don't know what I was thinking.' This is why suicide prevention is so important: because people can be very persuasive in arguing why they believe life—their life—is not worth living. And yet the situation looks radically different months later, sometimes because of an antidepressant, sometimes because of a change in circumstances, sometimes just a mysterious change of mind."

If you have suicidal thoughts, call the National Suicide Prevention Lifeline at 800-273-8255 or phone a family member or friend. And wait it out, knowing that in time you will most likely experience one of these mysterious changes of mind and once again yearn for life. SA

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Illustration by Izhar Cohen

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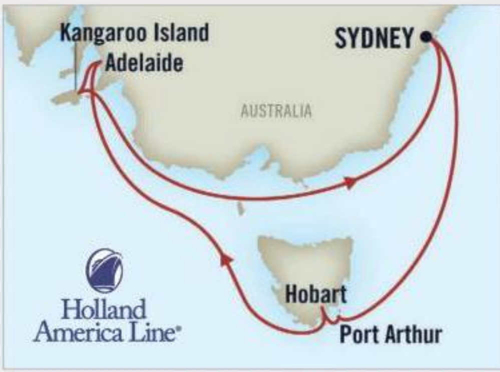

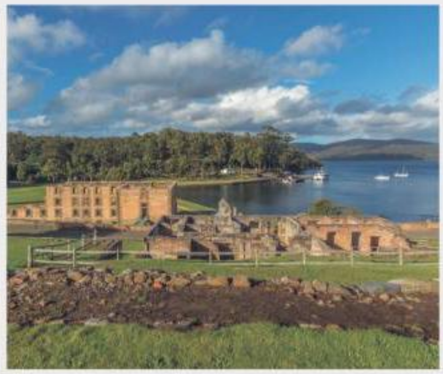

SPEAKERS:

Alex Filippenko, Ph.D.

Alex Filippenko is an elected member of both the National Academy of Sciences and the American Academy of Arts & Sciences, is one of the world's most highly cited astronomers and the recipient of numerous prizes for his scientific research. He was the only person to have been a member of both teams that revealed the accelerating expansion of the Universe, an amazing discovery that was honored with the 2011 Nobel Prize in Physics to the teams' leaders and the 2015 Breakthrough Prize in Fundamental Physics to all team members. Winner of the most prestigious teaching awards at UC Berkeley and voted the "Best Professor" on campus a record nine times, he was named the National Professor of the Year in 2006. He has produced five astronomy video courses with The Great Courses, coauthored an award-winning astronomy textbook, and appears in more than 100 television documentaries. In 2004, he was awarded the Carl Sagan Prize for Science Popularization. He was recently selected as one of only two recipients of the 2017 Caltech Distinguished Alumni Award.

Martin Green, Ph.D.

Martin Green is Scientia Professor at the University of New South Wales, Sydney and Director of the Australian Centre for Advanced Photovoltaics, involving several other Australian Universities and research groups. His group's contributions to photovoltaics are well known and include holding the record for silicon solar cell efficiency for 30 of the last 34 years, described as one of the "Top Ten" Milestones in the history of solar photovoltaics. Major international awards include the 1999 Australia Prize, the 2002 Right Livelihood Award, also known as the Alternative Nobel Prize the 2007, SolarWorld Einstein Award, and, most recently, the 2016 Ian Wark Medal from the Australian Academy of Science.

Angela Moles, Ph.D., F.R.S.N.

Angela Moles is a plant ecologist at UNSW Sydney. Angela studies global patterns in the ways plants grow. One of Angela's studies, known as "The World Herbivory Project" took her to 75 ecosystems around the world, including arctic tundra in Greenland and Alaska; deserts in Arizona; Central Australia and Israel; tropical rainforests in the Republic of Congo, Panama, China, Mexico and Peru; shrublands in Mexico and California; temperate forests in Argentina, Sweden, Tasmania, Norway, and Oregon; and savannas in South Africa, Australia, and Zambia. At each site, Angela and her team measured how well defended the plants were, and how much of their leaf area was eaten by animals. This study overturned the long-held idea that plants are better defended in the tropics (they are actually better-defended at higher latitudes), and the idea that plants suffer greater losses to animals in tropical ecosystems (plants get eaten a lot everywhere).

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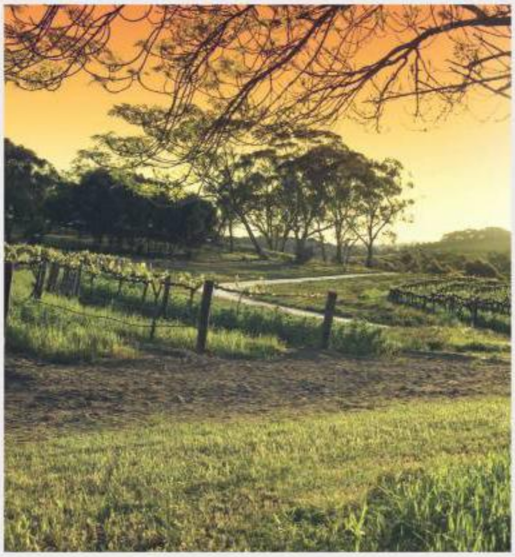

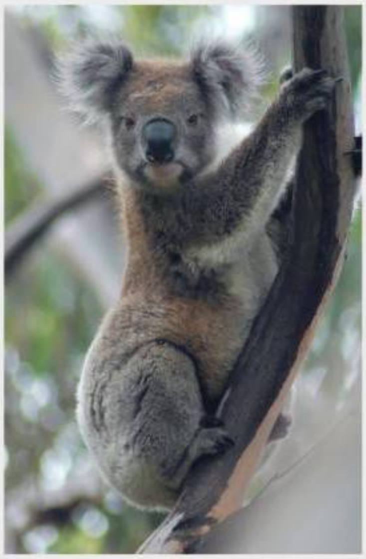

Since having children, Angela has stopped travelling so much and started working on introduced species. Angela's group has shown that 70% of the annual plant species introduced to Australia in the last 100 years have changed significantly since their arrival from overseas. A glasshouse study on a beach daisy introduced to Australia from South Africa in the 1930s has revealed substantial differences in growth form, flower size and photosynthetic rate between the South African and Australian forms of this plant, and the two populations do not cross to form strong offspring.

Veena Sahajwalla, Ph.D., F.T.S.E.

Australian Research Council (ARC) Laureate Professor Veena Sahajwalla is revolutionizing recycling science to unlock the wealth of resources in the many complex and toxic wastes currently destined for landfill. As a materials scientist and engineer and founding Director of the Centre for Sustainable Materials Research and Technology (SMaRT) at the University of New South Wales, Sydney, she is producing a new generation of green materials, products and resources made entirely, or primarily, from waste.

Veena Sahajwalla is an internationally respected scientist and engineer. Her research focuses on the sustainability of materials and processes with an emphasis on environmental and community benefits. One of her most celebrated achievements is the invention of a process of recycling plastics and rubber tires in steelmaking, now known around the world as green steel. Veena has published around 300 peer-reviewed papers and delivers keynote and invited speeches across Australia and worldwide.

She continues her community engagement through regular school visits and public talks, her mentoring program for girls in science (Science 50:50) and regular media commentary. In 2017, Veena Sahajwalla received the 2017 PLuS Alliance Prize for Research Innovation category and became the first woman to be awarded the prestigious Jubilee Professorship by the Indian Academy of Sciences.

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- Global Patterns in Plant Defense
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Steve Mirsky has been writing the Anti Gravity column since a typical tectonic plate was about 36 inches from its current location. He also hosts the *Scientific American* podcast Science Talk.

True Story

Look, I know what I know. I think

By Steve Mirsky

I distinctly remember the moment when I started to feel my mind go. It was Tuesday, July 31. Or what happened was that day, and I heard about it the next day. Or I saw it live as it happened. Those details are not important. The only important thing is that I remember it distinctly. President Donald J. Trump was at a rally in Florida, explaining the need for strong voter-identification laws. "You know, if you go out and you want to buy groceries, you need a picture on a card, you need ID," he said. "You go out and you want to buy anything, you need ID and you need your picture."

I had, of course, heard the president say many, many things over the years that were true … I mean, not true. The *Washington Post* tallied 4,229 "false or misleading claims" by Trump in his first 558 days in office. Can you believe that? I could. Before my mind went.

Here's an example of my conundrum. Early this year, Trump refuted the idea of climate change: "The ice caps were going to melt, they were going to be gone by now, but now they're setting records, so okay, they're at a record level." But a researcher at the National Snow and Ice Data Center said that polar ice was at "a record low in the Arctic (around the North Pole) right now and near record low in the Antarctic (around the South Pole)." The Trump claim and the response were both published by the Pulitzer Prize–winning organization PolitiFact. But I don't know anyone there.

I was reading a book. The book is called *The Death of Truth*. The writer's name is Michiko Kakutani. She wrote that the Trump administration ordered the Centers for Disease Control and Prevention to avoid using the terms "science-based" and "evidence-based." She says that in another book called *1984* there's a society that does not even have the word "science" because, as she quoted from that other book, "'the empirical method of thought, on which all the scientific achievements of the past were founded,' represents an objective reality that threatens the power of Big Brother to determine what truth is." Is what she wrote true? I don't know. And why can't two plus two be five? Or three. Or both at the same time. That's true freedom.

Kakutani also wrote that a man named Rush Limbaugh was on the radio and said that "The Four Corners of Deceit are government, academia, science and the media." In my country, we're supposed to have government "by the people." So I think I might be in the government. And I have been in academia. And I have a job in media covering science. I feel shame.

Maria Konnikova is a science journalist. She also has a doctorate in psychology. So she should feel shame, too. She wrote an article for a place called Politico entitled "Trump's Lies vs. Your Brain." She wrote, "If he has a particular untruth he wants to propagate … he simply states it, over and over. As it turns out, sheer repetition of the same lie can eventually mark it as true in our heads." She also wrote that because of how our brains work, "Repetition of any kind—even to refute the statement in question—only serves to solidify it."

Anyway, groceries. I was sure that I had bought groceries at some point during the week before the president said that I would have needed to show a picture ID to buy those groceries. And I did not remember showing or even being asked to show a picture ID to buy those groceries. The cashiers usually only wanted pictures of Alexander Hamilton or Andrew Jackson against a green background—these pictures are money. Or my credit card, which does not have my picture on it. I'd need to look at it again to say for sure whether it has my picture on it.

And so I started to remember showing my photo ID to buy groceries. Everything was all right. The struggle was finished. I had won the victory over myself. I loved Big Lying. SA

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Illustration by Matt Collins

50, 100 & 150 YEARS AGO

INNOVATION AND DISCOVERY AS CHRONICLED IN *SCIENTIFIC AMERICAN*

Compiled by Daniel C. Schlenoff

OCTOBER

1968 Radio-Wave Astronomy

"Almost exactly a year ago a small group of workers operating a new radio telescope at the University of Cambridge were surprised to find that weak and spasmodic radio signals coming from a point among the stars were, on closer inspection, a succession of pulses as regularly spaced as a broadcast time service. With skepticism bordering on incredulity, the Cambridge group began systematic observations intended to reveal the nature of these strange signals. After all, seasoned radio astronomers do not make the mistake of supposing that every queer signal on their records is truly celestial; in 99 cases out of 100, peculiar 'variable radio sources' turn out to be some kind of electrical interference—from a badly suppressed automobile ignition circuit, for example, or a faulty connection in a nearby refrigerator. We finally concluded that the only plausible explanation for these mystifying radio sources was that they were caused in some way by the vibrations of a collapsed star, such as a white dwarf or a neutron star. —Antony Hewish"

Hewish shared the 1974 Nobel Prize in Physics for his research in radio astrophysics.

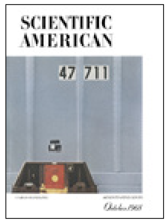
1918 Defense against Poison Gas

"There is no place in trench warfare for individual oxygen tanks. Accordingly, the gas mask is not a respirator providing an artificial atmosphere for the wearer to breathe; it is a sieve making the poisoned air about him fit for his use. In the beginning it was simple enough to design a mask that would do this. The Germans were using only chlorine gas, and this is a very active chemical; it will combine with almost anything in the world. It was easy to find a competent reagent for such a gas, and to place a sufficient quantity of it in the masks. But as the chemist made more of a specialty of the poison-gas field, and introduced more variety into his attack, an equally inclusive defense became necessary. After exhaustive tests, the chemists find that first rank must be given to charcoal produced from peach stones, the pits of apricots, olives and cherries, and the shells of brazil nuts and walnuts. Every mask requires seven pounds of seeds and shells."

1868 Sugar and Slavery

"From a correspondent in Havana, Cuba, Ezra K. Dod, we have received a communication relating his experiences on sugar estates on the 'ever faithful Isle,' and asking for improvement in our sugar interests. 'It is well known that in France the cost of manufacture has been reduced in greater ratio than the fall in price, and the business is profitable, while here the cost of production and manufacture is now more than it was in 1830, as negroes have nearly tripled in value. I do not think there is an estate on the island that pays current expenses. The amount of depreciation of lands, buildings, etc., leaves but about $150 per year for each negro; a sum not sufficient to cover the interest on their cost, deaths, and yearly depreciation, and yet the cry is, more hands.'"

Slavery was not completely abolished in Cuba until 1886.



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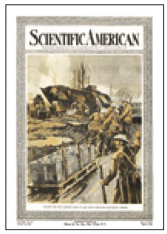
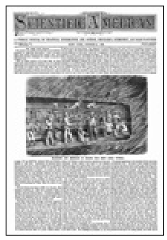


1918


1868

Taking a Stand on Darwin

"Dr. J. D. Hooker, in his recent address to the British association at Norwich, says: 'Ten years have elapsed since the publication of "The Origin of Species by Natural Selection," and it is hence not too early now to ask what progress that bold theory has made in scientific estimation. The scientific writers who have publicly rejected the theories of continuous revolution or of natural selection take their stand on physical grounds, or metaphysical, or both. Of those who rely on the metaphysical, their arguments are usually strongly imbued with prejudice, and even odium, and, as such, are beyond the pale of scientific criticism. Having myself been a student of moral philosophy in a northern university, I entered on my scientific career full of hopes that metaphysics would prove a useful Mentor, if not quite a science. I soon, however, found that it availed me nothing, and I long ago arrived at the conclusion, so well put by Louis Agassiz, where he says, 'We trust that the time is not distant when it will be universally understood that the battle of the evidences will have to be fought on the field of physical science and not on that of the metaphysical.'"

1918: An American dispatch rider steers his motorcycle through a "gas soaked" village near the front lines in Europe. He wears an early protective hood against poison gas.

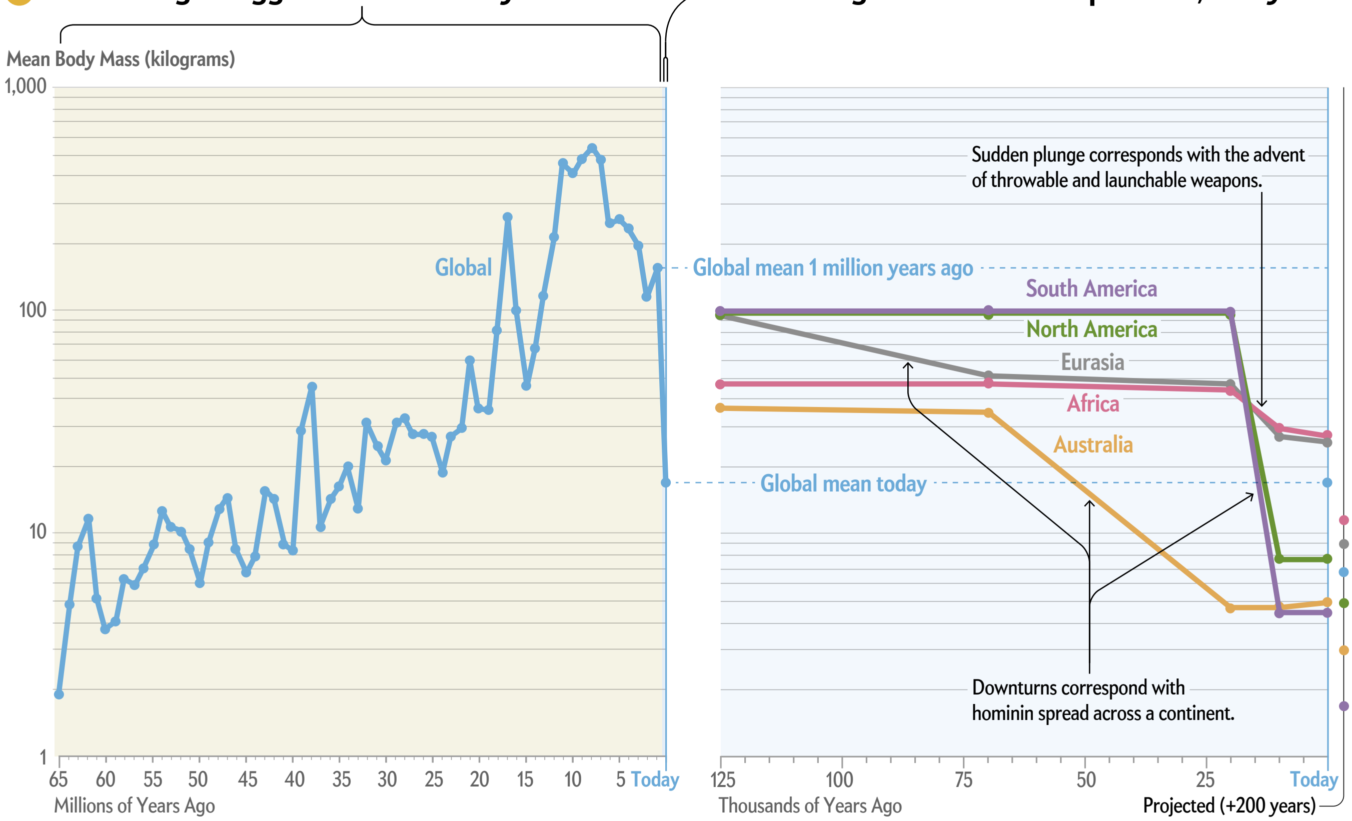
SCIENTIFIC AMERICAN, VOL. CXIX, NO. 15; OCTOBER 12, 1918

Text by Mark Fischetti | Graphic by Lucy Reading-Ikkanda

Honey, I Shrunk the Mammals

Where humans migrate, mammals become smaller

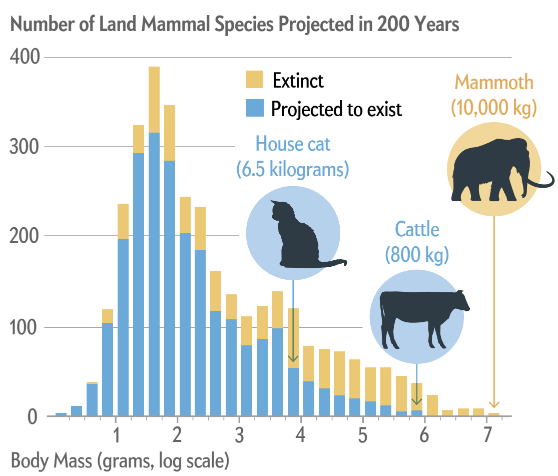
A Mammals got bigger for 65 million years → **Mammals got smaller in the past 125,000 years**



For millions of years the extinction rates among large, medium and small land mammals were similar. Yet the large species started dying off much faster, about 100,000 years ago in Eurasia, 50,000 years ago in Australia, and 15,000 years ago in North and South America (A). These shifts, it turns out, correspond with when a hominin species—*Homo erectus, Homo neanderthalensis* and especially *Homo sapiens*—spreads across a continent. "There is an astoundingly tight fit" among the data sets, says Felisa A. Smith, a paleoecologist at the University of New Mexico, who led the research. Hefty animals suffered from being hunted, as well as habitat change and fires caused by human activities. The imbalance continues today, leaving far fewer massive animals, even though small ones go extinct, too. Two centuries from now, cows may top the size chart (B). "We have changed the entire Earth," Smith says. "Now we have to be nature's stewards."

B Cows Rule the Future

In 200 years, elephants could be gone, and cattle could be the biggest beasts remaining on land—if humans continue aggressive hunting and habitat destruction.



SOURCE: "BODY SIZE DOWNGRADING OF MAMMALS OVER THE LATE QUATERNARY," BY FELISA A. SMITH ET AL., IN *SCIENCE*, VOL. 360; APRIL 20, 2018