SPEAKING IN WHISTLES — PAGE 60
WHAT'S WRONG WITH COSMIC INFLATION? — PAGE 32

SCIENTIFIC AMERICAN

WORKOUTS AND WEIGHT LOSS

Learn the surprising evolutionary reason why exercise alone won't shed pounds—and what to do about it

PLUS

PREVENTING THREATS TO CROPS
Airborne microbes' critical role PAGE 40

WHAT IS A KILOGRAM?
Science seeks new ways to ensure accuracy PAGE 46

MEDICAL SCANS
A shortage of rare atoms imperils disease imaging PAGE 68

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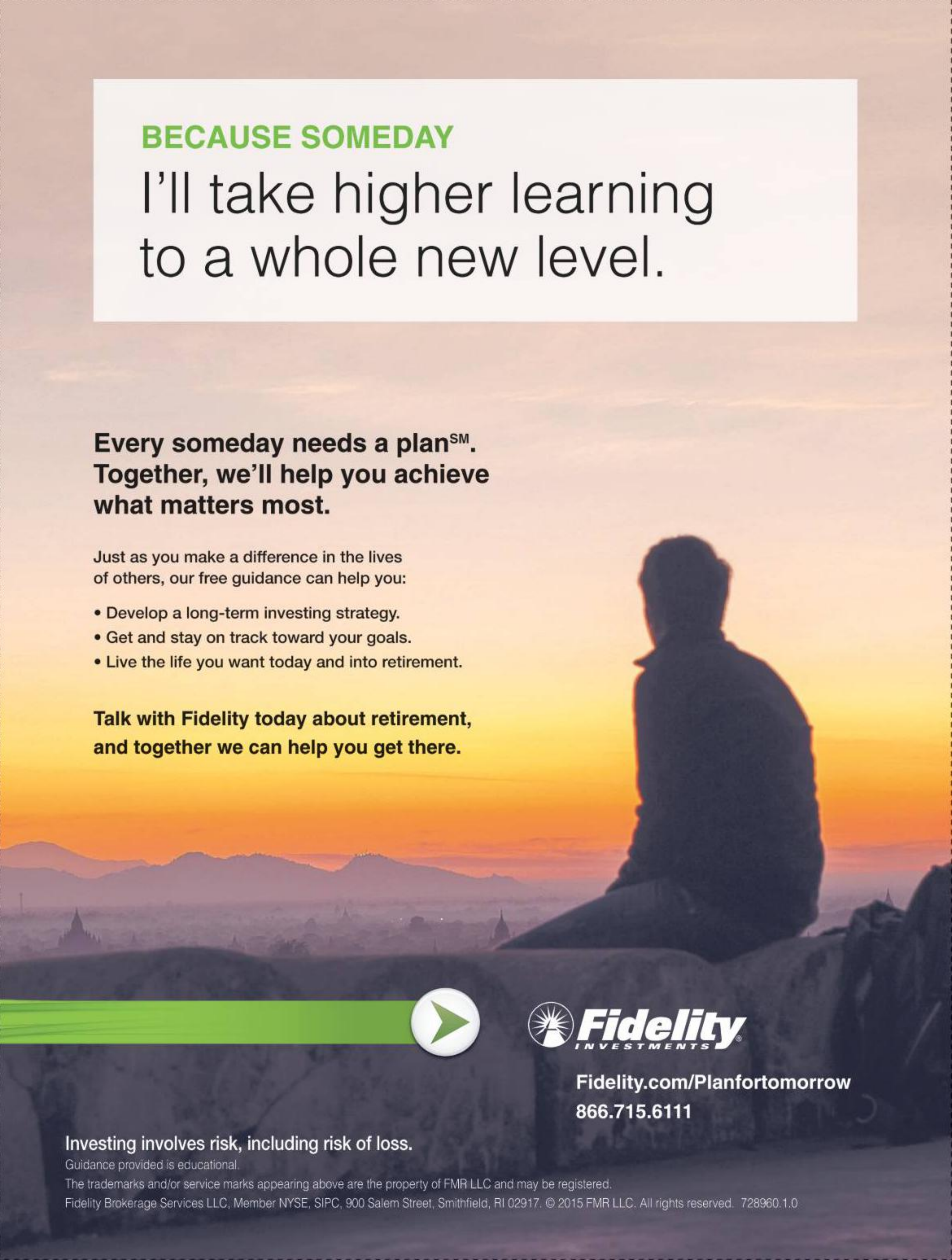
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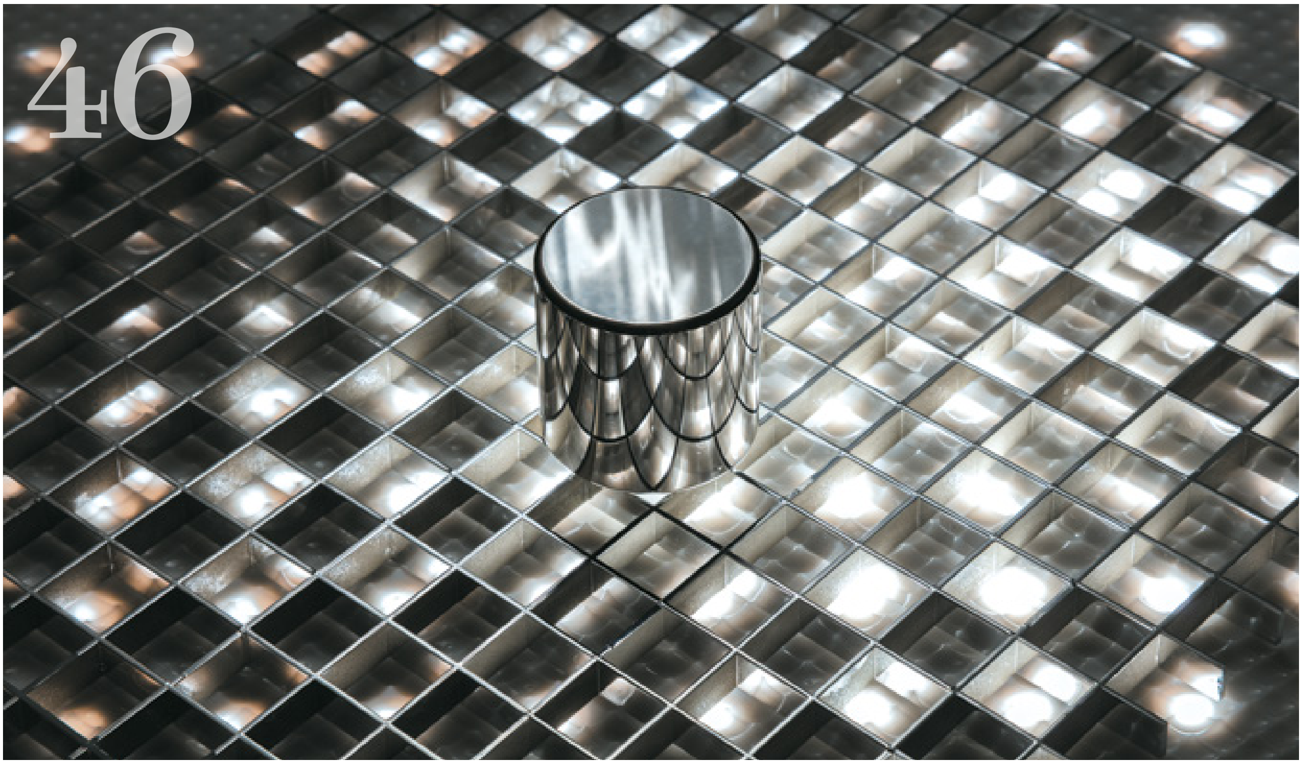

ON THE COVER

We take it for granted that physically active people burn more calories then sedentary folks. But studies show that daily energy expenditures are largely the same regardless of activity level. The findings help to explain why hitting the gym to lose weight does not work and raise intriguing questions about human evolution. Illustration by Bryan Christie.

Photograph by Richard Barnes

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ON THE WEB

Trump's First 100 Days
Scientific American explores the potential impact of the newly elected president's first 100 days in office on science and technology.
Go to www.ScientificAmerican.com/feb2017/first-100

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PROMOTION

The Agenda Setters

Bringing Science to Life

The Future of Oral Health

The Lambs Club | New York City | November 28, 2016

As part of an ongoing partnership with Colgate, Scientific American's Custom Media Division recently showcased the innovation driving oral health at a breakfast gathering in New York.

Members of the oral healthcare community, as well as policy and media thought leaders, discussed how global challenges, advances and new technologies are shaping the future of oral health. The forum featured such luminaries as **Michael C. Alfano** (Santa Fe Group and New York University), **Marko Vujicic**, (American Dental Association) and **Sharon Guynup** (Editorial Director, *The Future of Oral Health*). **Jeremy Abbate** (VP & Publisher, Scientific American) moderated the discussion; **Ian M. Cook**, CEO of Colgate-Palmolive, gave opening remarks.

Learn more at: **scientificamerican.com/futureoforalhealth**

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

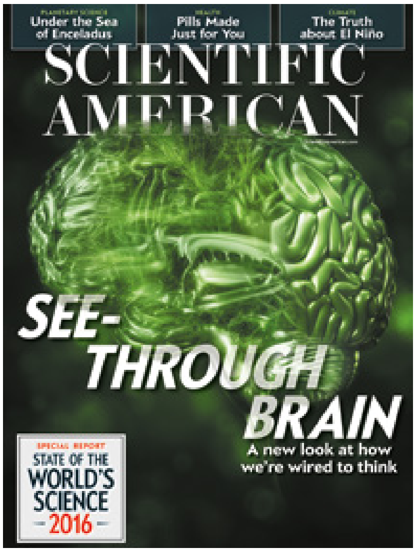
From Workouts to Far Out

Many people I know (including members of my family) feel exercise is a time-consuming, unpleasant chore, and they dread it. The need to change into other clothes, to frequently take a block of time out of busy lives, and to get dirty and fatigued: they find it all unappealing. But I've always enjoyed the hard work and even the satisfaction of earning the next day's sore muscles. And I indulged myself with a slight sense of pride in knowing not only that I was helping the biological machinery that promotes health but also that I got a nice side benefit of being able to eat cookies because I'd burned extra calories.

Wrong. Or, at least, not entirely right. As science shows over and over again, our intuitive notions about how things work often don't stand up in the face of data and careful analysis. The benefits of exercise are a case in point. In this issue's cover story, "The Exercise Paradox," anthropologist Herman Pontzer describes a surprising and fascinating result of evolution: humans burn about the same number of calories regardless of activity level. And compared with other animals, we use a lot of calories. In addition to overturning our commonsense notions, the findings provide further insights about why our kind has been so extraordinarily successful, becoming the dominant force on the planet. By the way, to be clear, we should all exercise. Regular activity does help our inner engines run right, and it has some nifty perks in elevating mood and improving cognition. But enabling weight loss regardless of diet? Not so much. Turn to page 26.

The knowledge that we have had the capability to rule over our own world has inspired the idea that we would someday also come to live on other planets. To be sure, that knowledge encompasses healthy amounts of romanticism, a sense of adventure and even concerns about having sufficient options to ensure our species' long-term survival. Unfortunately, the "easy" problems of longer space journeys include such seeming trivialities as escaping Earth's gravity with rockets, building airtight ships with enough air to breathe, and carrying huge amounts food and water. A much harder challenge is one that Hollywood never told you about: the perils to the brain from cosmic radiation, which neuroscientist Charles L. Limoli describes in "Deep-Space Deal Breaker," starting on page 54. Will it prove to be the barrier to our conquering "the final frontier"? One thing is certain: our innate human ambition and ingenuity mean we won't stop trying. SA

Illustration by Bomboland (running figure); Illustration by Nick Higgins (DiChristina)



October 2016

> "The Drug Enforcement Agency's claim that heroin has no medical application ignores a long history of utility and responsible use."
>
> THOMAS W. FILARDO *ANN ARBOR, MICH.*

SCIENCE JOURNALISM

In "How to Spin the Science News," Charles Seife criticizes the practices of close-hold embargoes—in which sources for an article restrict access to particular publications and require that reporters not contact other, unapproved sources before a particular date—in science journalism.

There are too many pop-science journalists who misconstrue stories. How can scientific institutions ensure that their evidence-based information makes it to the public and that journalists do not prop up a dissenting, unscientific opinion in the name of so-called balance? Perhaps they have found a solution in the close-hold embargo.

Seife's examples of embargoes include fairly harmless stories, such as the California Institute of Technology giving particular journalists early access to a new finding because it wanted excellent reporters to cover it. Another is the unrepresentative case of a researcher with a history of bad science—who was not acting as part of a large governmental institution—giving early, close-hold access to a dubious paper. The paper was retracted, as expected. Most of the examples are from the Food and Drug Administration, such as one regarding a laudable antismoking campaign—largely seen as a success—and another listing invited journalists from across the political spectrum, including the *Wall Street Journal* and Politico. All are from 2014 or earlier, and no evidence is given that the FDA has continued the practice.

Can Seife provide any proof that the close-hold embargo has caused real harm or damage outside of hurt pride from excluded journalists? What we need from *Scientific American* these days is a concerted effort to promote scientific and academic institutions, not demonize them. And we need it to provide factual and evidence-based information rather than speculative conspiracy theories that erode the public's trust in academic pursuits.

DARCY CORDELL
via e-mail

I cannot think of a more fundamentally distressing situation than the muzzling of the scientific press as described in this article. The close-hold embargo has no place in scientific institutions of the government or academia.

THOMAS J. MARTIN
Woodbridge, Va.

SEIFE REPLIES: Cordell's statement that Scientific American *needs to make "a concerted effort to promote scientific and academic institutions, not demonize them," underscores a fundamental disagreement that people have about the role of the press when reporting on science. The implicit, and widely held, argument on one side is that the prime function of the science journalist is to promote the statements of mainstream scientific institutions and scientists, the better to inform the citizenry and defeat pseudoscience.*

That is a good part of what we do, but it is not our only role. Science journalists are expected to be critical of authorities, whether or not we generally approve of them. It is neither speculative nor conspiratorial to say that even the best scientific institutions operate in a political environment, and when they vie for funding and influence, their goals might diverge from what is best for the populace—and for science. This is the cold reality of what happens when science meets human ambition. Journalists don't serve our readers if we fail to keep check on the institutions that influence our lives and expend our nation's treasure.

The degree to which embargoes hamper that second function is a matter of debate even within the science journalism community. But as my article shows, close-hold embargoes influence coverage to the point where correspondents are unable to get independent (and necessary) voices before going to press. Unless journalists have the full freedom to exercise their critical function, they risk becoming little more than glorified public relations professionals. And I truly hope that is not what the vast majority of the audience wants or expects from Scientific American.

PERSONALIZED THERAPY

"The Right Pill for You," Dina Fine Maron's article on personalized genetic medicine, was a long-overdue breath of fresh air. I would like to add another important use of genetic drug matching, or pharmacogenomics: the possibility of stratifying patients in clinical trials based on their genomic variability. An approach that is limited to the individuals with a high potential to respond to a drug may take far less time and save patients and insurers large sums of money.

MEHRDAD NADJI
Professor of pathology
University of Miami

MEDICAL USE VS. ABUSE

"Our Senseless Pot Laws," by Carl Hart [Forum], criticizes the Drug Enforcement Administration for declining to reclassify marijuana from its status as a Schedule I drug, defined as one "with no currently accepted medical use and a high potential for abuse." That language is at direct odds not only with Hart's and others' cited research on cannabis and its several therapeutic effects but also in ignorance of nontrivial facts from other advanced nations' pharmacopeia.

The Schedule I drug diacetylmorphine, or heroin, provides a clear example of the DEA's denial politics. It is called diamorphine in the U.K. and elsewhere. The U.K. has used it for severe pain for decades, and it is still prescribed today. The DEA's claim that it has no medical application ignores a long history of utility and responsible use and aims a slur at responsible practitioners from other nations.

The current opiate overdose epidemic in the U.S. is being met with myriad potential remedies, but this effort cannot be successful if the fundamental definitions on which it is based are so devoid of cogent scientific basis.

Thomas W. Filardo
Retired director of clinical research
Ethicon Endo-Surgery
Ann Arbor, Mich.

STEM EDUCATION

Thank you for pressing the case for the humanities as part of the educational curriculum in "Science Is Not Enough" [Science Agenda]. I am currently winding down a long (40-year) career as a biostatistician. The one skill that was most valued by my various employers over the years was not my mathematics abilities but the fact that I wrote very well. I can thank all of my English teachers for encouraging this.

Dave Bodycombe
via e-mail

The editors accuse Kentucky governor Matt Bevin of proposing a "STEM-only curriculum" because he advocates state subsidies for students in scientific disciplines and not the humanities. No one is advocating that we abolish the humanities. This is a prudent use of resources to encourage students to pursue a career where their employment prospects are brightest. I say this as the father of a daughter with a master's in anthropology, a mountain of student debt and bleak job opportunities.

Greg Daniels
Sun Valley, Calif.

ERRATUM

"Under the Sea of Enceladus," by Frank Postberg, Gabriel Tobie and Thorsten Dambeck, incorrectly referred to a million kilometers per hour as about 1 percent of light speed. It is 0.1 percent.

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A Letter to Washington

Political leaders must spend the next four years solving tough problems based on shared values, not divisive ones

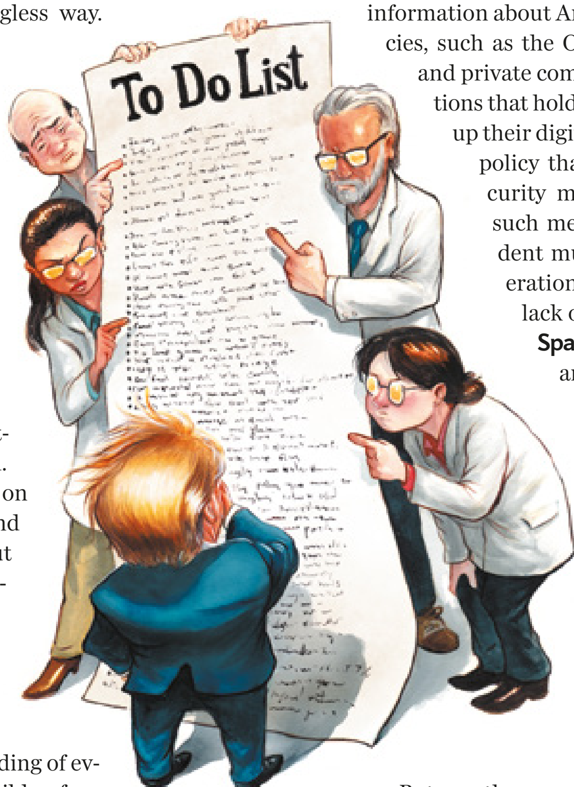
By the Editors

Dear President Trump and members of Congress:

As you took office in January, you came face-to-face with pressing problems involving science, medicine and technology that directly affect our country's health, wealth and security. They have often been ignored by your predecessors or simply "kicked down the road" in a meaningless way. Your critics fear that you will do something more dangerous: not simply defer crucial decisions but actively promote policies that ignore overwhelming scientific evidence about climate change, vaccines, national security and other issues. Some statements both from you as the incoming president and from majority party representatives in Congress about such topics have been worrisome.

But you have the opportunity to make real changes for the good of the whole nation, with actions using fact-based approaches and common ground.

We do not expect politicians elected on broad promises to shrink government and undo regulations to agree with us about the value of all policies. We are sure, however, that you would agree with President Dwight D. Eisenhower, who, when mobilizing the U.S. to deal with new threats in a post–World War II world and a changing economy, told the nation that "love of liberty means the guarding of every resource that makes freedom possible—from the sanctity of our families and the wealth of our soil to the genius of our scientists." The actions we list below not only guard those resources but will help them flourish.



Health costs: Start by giving Medicare, the nation's largest insurance program, the power to negotiate prices with pharmaceutical companies. Government on the federal and state level also needs to continue efforts to make health care affordable by reforming the Affordable Care Act to eliminate double-digit premium price hikes and by maintaining inexpensive insurance coverage for the millions who have obtained it already.

Earth and climate: NASA's ability to observe Earth helps us understand the way changing sea levels impact our defense forces and how groundwater shortages affect our farmers, not just to grasp the scope of global warming. We need to maintain both the money and the expertise to continue high-quality observations, no matter which agency carries them out.

Clean energy: The U.S. needs to implement the Clean Power Plan for power plants—under court review this winter—as part of our commitment to reduce greenhouse gas emissions, made during the international COP21 climate agreement in Paris.

Natural resources: Groundwater supplies, essential for crop irrigation and drinking water, are threatened by pollution. Protect them by giving the Environmental Protection Agency the resources to enforce newly enhanced laws governing toxic substances and chemical safety, as well as the Safe Drinking Water Act.

Cybercrime: Criminals have stolen important private information about Americans from government agencies, such as the Office of Personnel Management, and private companies, such as Yahoo. Organizations that hold such data must be made to shore up their digital vulnerabilities, either through policy that dictates specific high-level security measures or through penalties if such measures are not taken. The president must also seek international cooperation in combating attacks, given the lack of borders that exist online.

Space: Appoint a NASA administrator and determine the country's future space plans on a long-term basis, not one that changes with every election. Appoint a board of scientists charged with developing these goals, with terms that exceed those of an individual president or Congress.

These are not simple tasks, especially in a nation with the divided political values seen in the popular vote count of the November presidential election. But another president, the one who succeeded Eisenhower, inspired this country to choose to do things "not because they are easy but because they are hard." That chief executive, John F. Kennedy, told us that the tough challenges "measure the best of our energies and skills." When we succeed at them, when we craft policies that benefit our soil and rely on our science, they bring out the greatness in us all. SA

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Illustration by Scott Brundage

SIGNALLING A NEW APPROACH TO HEALTH

THE HUMAN GUT HOSTS TRILLIONS OF MICROBES. THE VAST POTENTIAL FOR MICROBIOTA MANIPULATION IN TREATMENT OF DISEASE IS ON THE CUSP OF MAJOR BREAKTHROUGHS.

SPRINGER NATURE
Yakult

Leaders in the fields of medicine, immunology, probiotics, microbiology and biochemistry presented the latest knowledge about host–microbiota interactions at the 18th Nature Café in Tokyo on 1 November. Their discussions explored future directions for microbiome research. After the presentations, a panel discussion moderated by **Dr Andrew Jermy,** chief editor of *Nature Microbiology*, raised questions about the challenges of defining the concept of a healthy microbiome. These events were held in conjunction with Yakult Central Institute Opening Conference.

THE RISE OF BIG DATA

The microbiome acts as a signalling hub, integrating information from the host such as genetic and immune signals with environmental factors such as lifestyle, diet and hygiene. A growing body of research shows that disruption of these signals in mice and humans leads to dysbiosis — an imbalance of microbiota that can develop into diseases.

For **Dr Eran Elinav** from the Weizmann Institute of Science, Israel, the challenge is to decipher the molecular basis of host–microbiome interactions, in the pursuit of personalizing medicine and nutrition.

Collaborating with mathematician and cell biologist, Eran Segal also at the Weizmann Institute, Elinav launched the Personalized Nutrition Project five years ago. This large-scale online initiative aims to identify factors that underlie blood glucose responses to food. The study has profiled more than 500 people, analysed more than 50,000 meals and monitored 2 million glucose measurements. The outcomes suggest that responses to food are highly individual. "A one-size-fits-all diet cannot be appropriate," says Elinav. "The gut microbiome is more unique than we thought."

In the long term, the project aims to develop personal dietary recommendations that may help prevent and treat obesity and diabetes. With obesity affecting 78 million adults and prevalence of Type II Diabetes currently estimated at half a billion worldwide, Elinav describes the conditions as "two of the worst epidemics in human history".

"The most important thing for the evolution of the microbiotic field in the near future will be a gradual shift from descriptions of microbiome composition and diseases to the demonstration of causality," he says.

A NEW DAWN FOR PROBIOTICS

When it comes to probiotics, strains matter. The idea that health effects of probiotics are strain-specific has long dominated the field. But this standpoint has been challenged by a growing body of work suggesting that the benefits of live microbes may be attributable to broader groups of microbes (across species or genera) rather than at the single-strain level. With more than 25 years experience in probiotics, **Dr Mary Ellen Sanders,** a consultant with Dairy & Food Culture Technologies, highlighted the concept of 'core' probiotic benefits. She pointed to a 2012 study by Ritchie and Romanuk that examined probiotic efficacy on gastrointestinal diseases. Pooling data from 74 studies and 84 trials involving more than 10,000 patients, the meta-analysis concluded: "Across all diseases and probiotic species, positive effects of probiotics were observed

nature café
nature.asia/naturecafe

ERAN ELINAV
Weizmann Institute of Science, Israel

VANESSA SPERANDIO
University of Texas Southwestern Medical Center, USA

COLIN HILL
University College Cork, Ireland

MARY ELLEN SANDERS
Dairy & Food Culture Technologies, USA

for all ages, single vs. multiple species and treatment lengths."

The regulatory implications of the evidence for core probiotic benefits are far-reaching. For example, the term 'probiotic' is currently restricted on food labels in countries of the European Union. However, given probiotic benefits, Sanders says: "It would not be misleading to consumers for strains of certain well-studied species to be called probiotic, even if there are no studies specifically on that strain." While safety is paramount, Sanders also calls for frameworks that enable consumers to "make decisions for themselves."

On the frontiers of microbiotic research, she comments: "The biggest gap in the research now is trying to understand whether we can reverse dysbiosis and thereby improve health."

MARY ELLEN SANDERS
WE'RE JUST BEGINNING TO UNDERSTAND THE RELATIONSHIP BETWEEN CERTAIN BACTERIA AND CERTAIN HEALTH CONDITIONS

MINING THE MICROBIOME FOR THERAPEUTICS

With the discovery of an increasing number of microbiome-derived responses to medical problems, it's smart to view the microbiome as "a vast reservoir of antimicrobial strategies" from which interventions can be "mined" and developed, says **Dr Colin Hill,** professor of microbial food safety in the School of Microbiology at University College Cork.

Novel anti-microbials in the form of bacteriocins and bacteriophages are of particular interest due to their ability to target specific pathogens. Many studies have shown that *Bifidobacterium* and *Lactobacillus* produce bacteriocins, and genome analysis has identified bacteriocin gene clusters. It has been shown experimentally that unusual bacteriocins produced by the strain *L. salivarius* UCC118 protect mice against *Listeria monocytogenes* infection. Such studies open the door to further possibilities of manipulating microbiota to protect hosts against infection.

Hill described how bacteriocins could play a role in farming and agriculture. One study demonstrated that introducing a bacteriocin-producing strain into the mammary glands of dairy cattle infected with bovine mastitis — one of the most common and punitive diseases globally in cattle — led to complete recovery within three days. Hill noted that administering broad-spectrum antibiotics to cattle renders milk unsuitable for consumption during and for a period after treatment. Using bacteriocins eliminates this drawback.

In future, Hill asserts that a greater focus on narrow-spectrum microbials will be key to identifying novel probiotics and therapeutics. "Medicine relies very heavily now on broad-spectrum antibiotics," he says. "We're in a very exciting phase of microbiome research, as we're just beginning to understand the relationship between certain bacteria and certain health conditions. Our goal is to understand them at the mechanistic level, so that we can redeploy them back into the gut or other tissues."

CROSS-TALK BETWEEN PATHOGENS, MICROBIOTA AND HOST CELLS

Gastrointestinal bacteria are known to communicate with one another by producing autoinducers — compounds similar to hormones in mammalian cells. These autoinducers form the basis of quorum sensing, a cell-to-cell signalling system that enables bacteria to adjust to a particular niche. **Dr Vanessa Sperandio**, professor of microbiology at the University of Texas Southwestern Medical Center, presented her latest findings on how these sophisticated signalling systems can be decoded to better understand the three-way conversation between pathogens, microbiota and the host.

For example, host hormones such as epinephrine and norepinephrine, which play a central role in the 'fight or flight' response, have been extensively reported to have a profound impact on gastrointestinal function. Pathogenic bacteria have been shown to exploit these signals to regulate their virulence.

Sugar sources are also thought to be important cues for pathogens to regulate expression of their virulence genes. Sperandio and her colleagues have deduced that the pathogen enterohaemorrhagic *Escherichia coli* (EHEC), responsible for diarrhoea outbreaks, utilizes fucose to modulate its virulence and metabolism.

Sperandio says that much remains to be discovered in the realm of inter-kingdom chemical signalling. "There is a movement towards understanding how these interactions are happening at the molecular level and how this knowledge can be exploited to develop new antimicrobial strategies, be they probiotics, prebiotics, vaccines or novel antibiotics."

THE HEALTHY FUTURE OF MICROBIOME RESEARCH

THE PRESENTERS GIVE THEIR VIEW ON FUTURE DIRECTIONS FOR MICROBIOTIC RESEARCH.

The intestinal microbiome is increasingly recognized as a vast biochemical resource, with the potential to influence almost all aspects of our health and propensity for disease. Panellists at the 18th Nature Café in Tokyo concurred that discovering not just what happens in the gut, but underlying mechanisms, will be critical for development and for evaluating therapeutic interventions.

Most microbiotic research has focused on digestive health, and will continue to do so. 'Dysbiosis' is associated with a decrease in diversity of bacteria and Dr Kenya Honda from Keio University School of Medicine in Japan believes the challenge is to learn how to restore diversity.

"Bacterial cocktails consisting of around 20 to 30 strains may become effective," he said. "These may even arise within the next couple of years."

Panellists also agreed that future microbiome research will also consider how our intestinal symbionts influence other areas of health.

Mary Ellen Sanders, a consultant with Dairy & Food Culture Technologies, said she believes investigation of gut–brain interactions may become more prominent. Many companies and institutions are now exploring how gut microbiota may influence neurological, immunological, or endocrinological functions.

"There may be new ways to treat depression, anxiety and other disorders," she said.

Novel therapeutics mined from the gut may also be on the horizon. According to Colin Hill, professor of microbial food safety in the School of Microbiology at University College Cork, "it could be that the first applications of microbiome-derived anti-infectives will be in feed [for cattle, pigs and chickens]" rather than in food or medicine for human consumption.

The panellists agreed that a collaborative approach will be key to realizing the potential of microbiotic research.

There is "no better field than the microbiome" to illustrate the importance of collaboration, said Eran Elinav, principal investigator at the Weizmann Institute of Science. "This is a truly integrative field, so to grasp the importance of the microbiome, to study it mechanistically, one has to rely on collaborations between labs, which makes it complicated, but also much more fun."

Clues for gut health in early life

TAKAHIRO MATSUKI
Yakult Central Institute

As soon as we are born bacteria start colonizing our digestive tracts and begin flourishing into unique microbial ecosystems. Research increasingly suggests that the make-up of our microbiomes influences lifelong health. Although bifidobacteria are known to be among the first to colonize the human intestine, how they come to dominate the infant gut has remained unclear.

In a world-first study published in *Nature Communications*, a Japanese research team led by Takahiro Matsuki at Yakult Central Institute found that fucosyllactose, a component of the sugars found in breast milk, plays a crucial role in bifidobacteria colonization.

By tracking changes in microbiota composition during the first month of life and using genomic analysis, the researchers identified a bacterial gene that mediates fucosyllactose uptake into bacterial cells. The study is the first of its kind to propose that a single bacterial gene may influence the composition of intestinal microbiota. The finding opens new avenues for developing infant-targeted probiotics, promoting a healthy gut from birth.

Reference

Matsuki, T. *et al.* A key genetic factor for fucosyllactose utilization affects infant gut microbiota development *Nat. Commun.* 7:11939 doi: 10.1038/ncomms11939 (2016).

MEMORIAL LECTURE

YAKULT CENTRAL INSTITUTE OPENING CONFERENCE

KENYA HONDA, PROFESSOR, KEIO UNIVERSITY SCHOOL OF MEDICINE

KENYA HONDA
Keio University School of Medicine, Japan

The development and function of gut immune cell populations are influenced by components of microbiota. In particular, T helper type 17 (Th17) cells constitutively exist in the intestinal lamina propria and their accumulation depends on the presence of gut microbiota. We know that the induction of Th17 cells is controlled not just by the presence of bacteria, but by the composition of intestinal microbiota and, presumably, the presence of specific bacterial taxa for Th17 generation.

From a collection of murine intestinal bacterial stocks provided by Dr Umesaki of Yakult and Dr Itoh, formerly of the University of Tokyo, researchers used a gnotobiotic technique to screen for "Th17-inducing bacteria". The process involves comparing germ-free mice with defined microbiological status. A strong induction of Th17 cells was seen in the small intestine of mice monocolonized with segmented filamentous bacteria (SFB).

SFB were identified more than 30 years ago as spore-forming gram-positive bacteria with segmented and filamentous morphology. One of the characteristic features of SFB is their tight adhesion to epithelia. Now, we have identified these classical SFB as a component of the mouse microbiota that strongly induce Th17 cells.

Scanning electron micrographs have confirmed the presence of SFB in the intestinal tract of Th17 cell-sufficient (Taconic SPF) mice, but not in Th17 cell-deficient (Jackson SPF) mice. It has also been demonstrated that SFB induce Th17 cells in the small intestine of JAX mice. In addition to SFB, we have identified a mixture of 20 human-derived strains of bacteria that can trigger induction of Th17 cells in the mouse colon. In SFB and 20 human-derived strains, adhesion of microbes to intestinal epithelial cells seems to be a major cue for Th17 cell induction.

Colonization of germ-free mice with a mixture of 46 strains of mouse *Clostridia* and 17 strains of human *Clostridia* have been shown to induce a marked accumulation of colonic regulatory T (Treg) cells and, notably, anti-inflammatory molecules including interleukin-10. These effects on the microbiota are thought to contribute to the prevention of allergy, colitis, and graft-versus-host disease (GVHD).

In contrast to epithelial cell-adhering bacteria such as SFB, the 17 strains of *Clostridia* are thought to promote Treg cell induction through the production of metabolites including short-chain fatty acids in the colonic lumen. More study of the mechanisms behind *Clostridia*-mediated induction of Treg cells is needed.

We have begun to investigate how oral bacteria affect the intestinal immune system. Every day, humans produce 1.5 litres of saliva, which contains a vast amount of oral bacteria. These bacteria pass through the intestine due to "colonization resistance" by gut microbiota. However, dysbiosis can lead to colonization of oral-derived bacteria and this is one of the earliest events seen in Crohn's disease (CD). We collected saliva samples from healthy donors and from patients with CD, which were inoculated into germ-free (GF) mice. A sample from one CD patient induced a marked increase in T helper type 1 (Th1) cells in the inoculated mice. By culturing cecal contents from mice inoculated with the CD patient saliva, we isolated eight bacterial strains. Of those, we showed only *Klebsiella pneumoniae* sufficiently induced Th1 cells. We propose that *K. pneumoniae* could be a taxonomic biomarker for CD.

Advances in understanding of the gut microbiome are built on collaboration. I would like to thank Kiyoshi Takeda at Osaka University, Yoshinori Umesaki, Akemi Imaoka, and Tatsuichiro Shima of Yakult, Kikuji Itoh of the University of Tokyo, Dan Littman at the New York University School of Medicine and Ivaylo Ivanov at Columbia University. I would also like to thank my colleagues, particularly Takeshi Tanoue and Koji Atarashi, and collaborators at Keio University, RIKEN, Okayama University, Nagoya University, Osaka University, the Broad Institute and the National Institutes of Health.

Michael E. Mann is professor of atmospheric science at Pennsylvania State University. His most recent book, with Tom Toles, is *The Madhouse Effect: How Climate Change Denial Is Threatening Our Planet, Destroying Our Politics, and Driving Us Crazy* (Columbia University Press, 2016). **Susan Joy Hassol** is director of the nonprofit Climate Communication. She recently co-authored "(Un)Natural Disasters: Communicating Linkages between Extreme Events and Climate Change," in the World Meteorological Organization's *Bulletin*.

Climate Trumps Everything

The new administration could cut greenhouse gases and achieve its economic goals all at once

By Michael E. Mann and Susan Joy Hassol

Of all the potential actions in Donald Trump's forthcoming presidency, none will have more long-lasting effects than those on climate change. Just four days after the Paris climate agreement went into force—the first comprehensive global deal to reduce heat-trapping pollution—the U.S. elected a president who has called climate change a hoax and vowed to "cancel" the Paris accord. Trump has said he would block the Clean Power Plan, which would reduce utilities' greenhouse gas emissions and is at the heart of the U.S. commitment to the agreement. And he promises to reinvigorate the fossil-fuel sector, just when global energy production is moving rapidly in the opposite direction, toward clean, inexpensive, renewable sources.

Not only would this agenda be disastrous for climate, it would actually undermine Trump's ability to achieve his own primary goals. First, climate change is not like other issues that can be postponed from one year to the next. The U.S. and world are already behind; speed is of the essence because climate change and its impacts are coming sooner and with greater ferocity than anticipated: 2016 was the hottest year on record by a large margin, and 2015 and 2014 set the previous records. Extreme weather events such as heat waves and heavy downpours are becoming more frequent and severe, as are related fires, droughts and floods.

Warming is also causing sea level to rise at faster rates. At high tide, ocean water stands in the streets of coastal cities such as Miami, and it taints groundwater. The coastal threat of stronger and more destructive hurricanes is growing, too. The costs of these increasingly common events are reaching into the billions of dollars. Most frightening are the likely tipping points in the climate system—thresholds beyond which unstoppable feedbacks kick in. We don't know exactly where such points of no return are until we've passed them. Every year that we delay action, we increase the risk of crossing dangerous thresholds, and we commit our generation and our children's to more devastating outcomes.

Second, because emissions anywhere result in climate change everywhere, we are part of a community of nations that must work together to tackle this global problem. The U.S. has always prided itself on being a leader, not a laggard. We were one of the first nations, along with China, to ratify the Paris Agreement, which is part of a larger international treaty signed by George H. W. Bush in 1992 (the United Nations Framework Convention on Climate Change). The Paris Agreement has rules, which we agreed to, including that once in effect, no country can withdraw from the agreement for at least four years. If our new president were to pull out, our country would be an international outlaw, with consequences for our status among nations. We would also be relinquishing the leadership that prompts China and other nations to reach for more ambitious emissions reductions. Instead the U.S. would become an impediment to progress.

Finally—and perhaps this is where all Americans can find common ground—the clean energy revolution is well under way. The rest of the world is no longer debating climate change; it is moving on with a rapid transition to carbon-free energy. Do we want to be left behind in the great economic revolution of the 21st century? Or do we want to compete in the clean energy race, improving our international competitiveness and making our nation even greater? Do we want to buy solar panels and wind turbines from China, or do we want to manufacture and sell them to China and everywhere else?

If the U.S. is to accomplish what Trump says he wants for our nation—economic growth, job creation, improved infrastructure and international respect—then we need to lead the world in clean energy research, development and deployment. In doing so, we would also be keeping our air and water clean, making our businesses more efficient, improving our health and protecting our children's future. Surely, these are values we can all agree on. SA

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ADVANCES

1

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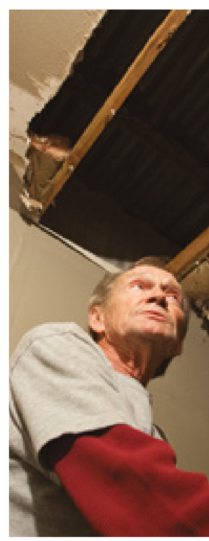
In the U.S., seismic activity and oil and gas production (*1*) have risen hand in hand over the past decade. Although most of the man-made tremors are small, the frequency of the quakes—and the damage they have incurred—has rattled residents in several states. Researchers, including from the University of Colorado Boulder (*2*), are seeking ways to quell the rumbling.

PRAGUE, OKLA., *March 2015*

COYLE, OKLA., *Jan. 2016*



INSIDE

McLOUD, OKLA., *Feb. 2016*

PAWNEE, OKLA., *Sept. 2016*

ENERGY

Man-Made Solutions for Man-Made Quakes

In a relatively short time, scientists have devised ways to manage human-induced earthquakes

In Oklahoma, Texas, Kansas and a handful of other states, oil and gas production has triggered a surge of earthquakes unlike anything scientists have ever seen. Oklahoma once had an average of one or two earthquakes a year, but in 2015 it had nearly 900. Meanwhile the rate of earthquakes in the central and eastern U.S.—long considered seismically quieter parts of the country—rose from 29 a year to more than 1,000.

The quakes have caused injuries, damaged homes and spawned class-action lawsuits. But given that oil and gas production is not expected to stop anytime soon, these seismic events probably won't either. In response, academic researchers, the federal government, energy companies and regulatory agencies have mobilized to try to reduce the frequency and strength of induced earthquakes—and a series of recent papers and other findings shows they have made rapid progress, although many questions remain.

Scientists have understood since the 1960s that injecting fluid into the ground at high pressure can cause earthquakes. In most cases, it is not hydraulic fracturing (or fracking) of oil- and gas-bearing rock that sets off tremors but the related process of wastewater injection. For instance, oil wells in Oklahoma—whether they are fracked or not—produce 10 or more barrels of groundwater for every barrel of oil. Companies separate the water and other by-products from the oil and inject it back into the ground via wastewater wells (a step designed to protect soil and surface water). But these injections can cause pressure that induces earthquakes by counteracting the friction that holds faults together. As Oklahoma and many other states entered the most recent energy boom, the amount of fluid pumped into wastewater wells grew rapidly.

In today's economic reality, whether wastewater injection should continue is off the table.

In today's economic reality, whether wastewater injection should continue is off the table. Researchers at Stanford University have turned instead to the question of *where* the injections should occur. So far they have mapped the natural geologic stresses throughout Oklahoma and Texas—the states with the largest populations at risk from human-induced quakes—and have discovered that only a fraction of faults hold the potential to slip in the presence of moderate pressure increases.

The team found that faults oriented in a certain direction, relative to natural tectonic stresses in the ground, are the ones most primed to become active. Faults that are critically stressed—that is, under enough natural force coming from just the right directions—may require a surprisingly small amount of additional force to rupture. (Compare this to a brick lying on a table. If you press down on the brick, it won't move. Nudge it from the side, however, and it will slide across the table.) That pressure can be as little as a few pounds per square inch (psi), says Jens-Erik Lund Snee, a Ph.D. candidate at Stanford and lead author of a Texas stress map published in October 2016 in *Geophysical Research Letters.* Lund Snee hopes that companies and regulators will pair these stress maps with fault maps to understand where wastewater injection will most likely cause earthquakes—and then steer clear of those areas.

One limitation of this study is that many earthquakes in Texas and Oklahoma have occurred on previously unmapped faults. Energy companies, however, may be able to use the Stanford team's data because they often have a better understanding of the subsurface than academic scientists or regulators. "It doesn't solve the problem, but it sure takes a big step toward solving the problem," says Heather DeShon, a seismologist at Southern Methodist University in Dallas who studies human-induced earthquakes.

Researchers are also investigating the benefits of installing dense networks of seismic monitors that could detect tiny earthquakes near wells. This could allow companies or regulators to take quick action to reduce injection volumes before the quakes grow larger, and Texas is currently installing such a network. Meanwhile some scientists suggest injecting waste liquid only into layers of the ground that are naturally sealed off from deep faults. Other experts are also making progress in figuring out exactly how much injection pressure different areas can tolerate before inducing seismic activity.

As scientists investigate pragmatic solutions, Oklahoma is still shaking. State seismologist Jake Walter says the various new findings will help in the long run, but he is focused on finding shorter-term answers. Since 2015 Oklahoma has slashed injection volumes and, in some cases, suspended wastewater disposal near seismic zones in an effort to mitigate the quakes. Although the state's earthquake rate subsequently slowed in 2016, the events have grown stronger in magnitude. Why? One explanation may be that as high-pressure pockets from wastewater injections continue to spread underground like a drop of water on a paper towel, they encounter new and sometimes larger faults. So even though there has been progress, Walter says, "We're not out of the woods yet."

—Anna Kuchment

TECHNOLOGY

Learn Morse Code, Semiconsciously

Wearable computers delivering tactile cues may offer a way to learn manual skills without paying much attention

Learning Morse code, with its tappity-tap rhythms of dots and dashes, could take far less effort—and attention—than one might think. The trick is a wearable computer that engages the sensory powers of touch, according to a recent pilot study. The results suggest that mobile devices may be able to teach us manual skills, almost subconsciously, as we go about our everyday routines.

Ph.D. student Caitlyn Seim and computer science professor Thad Starner of the Georgia Institute of Technology tinker with haptics, the integration of vibrations or other tactile cues with computing gadgets. Last September at the 20th International Symposium on Wearable Computers in Heidelberg, Germany, they announced that they had programmed Google Glass to passively teach its wearers Morse code—with preliminary signs of success.

For the study, 12 participants wore the smart glasses while engrossed in an online game on a PC. During multiple hour-long sessions, half the players heard Google Glass's built-in speaker repeatedly spelling out words and felt taps behind the right ear (from a bone-conduction transducer built into the frames) for the dots and dashes corresponding to each letter. The other six

PRECEDING PAGES: J PAT CARTER *Getty Images (pumping unit, Coyle, McLoud)*; RJ SANGOSTI *Getty Images (field researcher)*; NICK OXFORD *Redux Pictures (Prague)*; DAVID BITTON *AP Photo (Pawnee)*; THIS PAGE: GETTY IMAGES

participants heard only the audio, without the corresponding vibrations.

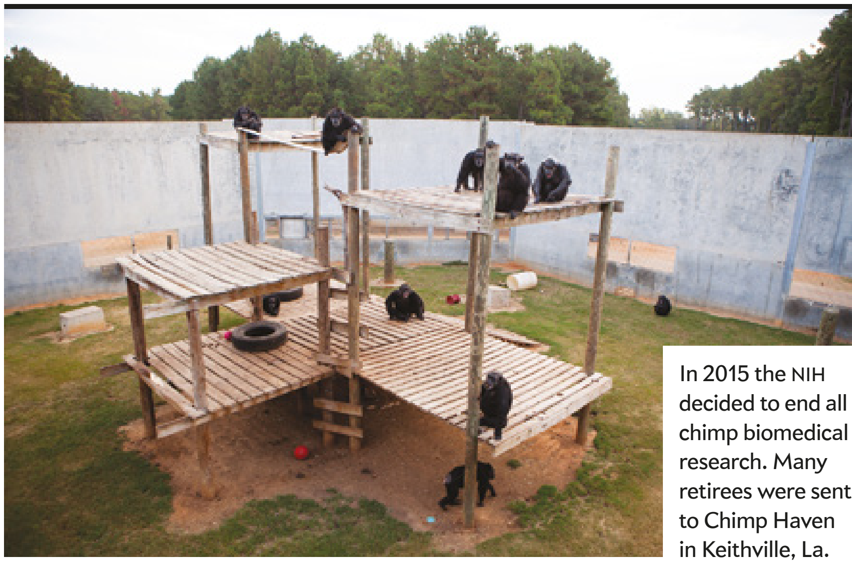
After each run of game playing, all the players were asked to tap out letters in Morse code using a finger on the touch pad of the smart glasses; for example, if they tapped "dot-dot," an "i" would pop up on the visual display. The brief testing essentially prompted them to try to learn the code. After four one-hour sessions, the group that had received tactile cues could tap a pangram (a sentence using the entire alphabet) with 94 percent accuracy. The audio-only group eventually achieved 47 percent accuracy, learning solely from their trial-and-error inputs.

The work shows that "it is possible to teach a system of typing without the user paying much attention to it," Starner says. Passive haptic learning could help users quickly master new text-entry methods for accessory keyboards or an eyes-free, Morse code–like system of taps on a smart watch, he adds, noting: "That might really change how people use mobile and wearable devices."

The results are also "exactly congruent" with other effects of passive haptic learning that the researchers have found in past studies, Seim says. For example, the group has developed computing gloves that deliver vibrations to the fingers to teach the "muscle memories" for playing a piano song or typing Braille.

Although it was small scale, the experiment demonstrates how wearable computers could permit users to "go about your daily business—and while you do that, you can get information to actually learn things," says Paul Lukowicz of the German Research Center for Artificial Intelligence, who was not involved in the study. Now if only listening to Mandarin in your sleep could impart fluency.

—Ingfei Chen



In 2015 the NIH decided to end all chimp biomedical research. Many retirees were sent to Chimp Haven in Keithville, La.

MELANIE STETSON FREEMAN *Getty Images*

ETHICS

To Treat Primates More Humanely: Transparency

Scientists look to open-data initiatives to lessen the burden of research on our closest animal relatives

Last year Congress issued a moral call to action when it ordered the National Institutes of Health to reevaluate its ethical oversight of government-funded primate research. Although the scientific community widely sees nonhuman primates as essential for advances in biomedicine (they have facilitated major gains in the fights against AIDS and neurological diseases such as Parkinson's, for example), researchers agree more can be done to treat the animals more humanely and conduct research less wastefully. To that end, the NIH gathered prominent scientists and ethicists last September to discuss the future of primate-based research—and they agreed that data sharing is the way forward.

Researchers could reduce experiments on nonhuman primates by studying data that have already been collected to answer new questions, says David O'Connor, a pathologist at the University of Wisconsin–Madison. O'Connor is walking the walk: his laboratory studies the Zika virus in primates, and he immediately posts all the results online. The goal is to figure out ways to combat Zika as quickly as possible without placing an undue burden on research primates.

The Seattle-based Allen Institute for Brain Science, which uses rhesus macaques to study the molecular basis of brain development, also makes all results public. O'Connor says this practice should be more widespread so that "researchers who are using this scarce but vital resource can learn as much as possible from as few animals as necessary." Still, he is skeptical that data sharing will catch on because it would require a change in "normative behavior"—science's strong culture of secrecy, in which data are kept under wraps until they are published in a peer-reviewed journal.

One step toward full transparency is to follow the lead of human clinical trials, says Christine Grady, a bioethicist at the NIH. U.S. law requires most clinical trials to register online and make their results public, even if a study fails or is inconclusive. This ensures that other researchers can learn from a trial regardless of its results—a move that could also safeguard primates against being used for the same thing twice.

Nancy Haigwood, director of the Oregon National Primate Research Center, also says data sharing is "the way of the future." Her center hosts 4,800 primates—including macaques, baboons and squirrel monkeys—to study a variety of human diseases. She currently contributes results from her center to O'Connor's Web site. "I don't see a downside," she says. "We have to share data more quickly." *—Monique Brouillette*

TECHNOLOGY

Bots in Your Bloodstream

Chemists create micro swimmers that can be controlled by light

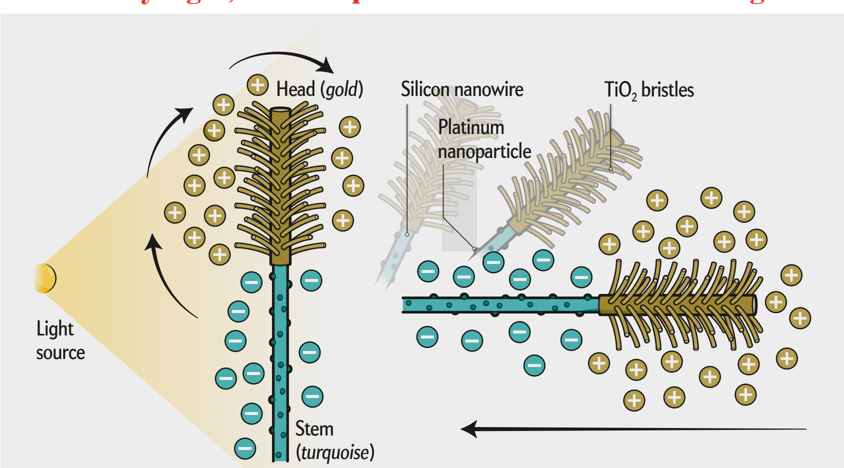
Microscopic machines that swim through the bloodstream to deliver drugs or perform minor surgeries have been a dream of scientists for decades. In the past 15 years researchers have created micro-engine variants that rely on chemical reactions, magnetism or vibration for thrust—but they often motor around erratically. The main challenge is guiding them to where they are needed, says University of Hong Kong chemist Jinyao Tang. Tang and his team have made progress on that front with a micro swimmer that can be smoothly and precisely steered with the help of light.

As reported in the December 2016 *Nature Nanotechnology,* the researchers built bottlebrush-shaped microparticles with silicon stems and titanium dioxide "bristle" heads. Both materials absorb photons, so when light is shined on the microparticle, the stem generates negative hydroxide charges and the bristles produce positive hydrogen ions. As the ions move to balance the uneven distribution of charge, they pull fluid with them, causing the micro swimmer to move toward the light—stem-first, like a dart.

As a test, researchers placed a swimmer in liquid on a glass slide and guided it with ultraviolet light to spell out the word "nano." The 11-micron-long motor could cover about a millimeter in two minutes—slow for medical applications—but Tang says they are now designing new geometries to speed up the swimmers. "This unique way of precisely controlling speed and direction is amazing," says Sámuel Sánchez, a nanoroboticist at the Max Planck Institute for Intelligent Systems in Stuttgart, who was not involved in the research.

This work is an early glimpse at medical robots that doctors could navigate through a patient's body from the outside with a focused beam of light, Tang says. The devices currently run on ultraviolet light—but the researchers are now working on micro swimmers that respond to a near-infrared wavelength, which can penetrate a few centimeters of tissue. For applications deeper in the body, surgeons could control the bots with optical fibers. *—Prachi Patel*

Led by Light, Microscopic Swimmers Could Deliver Drugs



Orientation
Light sets off chemical reactions on the surface of the micro swimmer, producing ions (charged particles). The head produces positive ions, and the stem generates negative ones. More ions are produced on the illuminated side than the shaded side, and this asymmetry causes the swimmer to turn so that it is oriented parallel to the path of the light.

Movement
The TiO_2 bristles give the head of the micro swimmer more surface area than the stem, so more positive ions are produced than negative ones. As the ions seek to rebalance the distribution of charge, the swimmer moves stem-first toward the light.

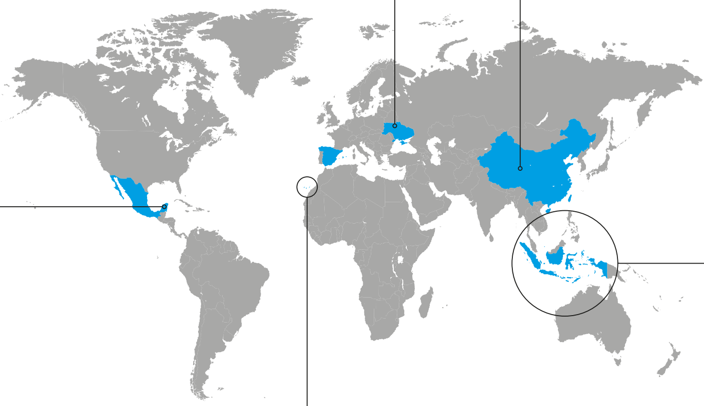
SOURCE: "PROGRAMMABLE ARTIFICIAL PHOTOTACTIC MICROSWIMMER," BY BAOHU DAI ET AL., IN *NATURE NANOTECHNOLOGY,* VOL. 11; DECEMBER 2016

Illustration by Brown Bird Design

IN THE NEWS
Quick Hits

UKRAINE
A 360-foot-tall steel and concrete hangar now covers Chernobyl's reactor 4, site of the 1986 nuclear meltdown. The structure replaced a leaking shield that was installed immediately after the disaster—and should prevent more radioactive debris from escaping.

CHINA
The first clinical trial to employ cells edited by the genetic tool CRISPR/Cas9 is now under way in China. Three more are scheduled to begin next month. In all four, humans are injected with modified immune cells that researchers hope will fight targeted cancers.



MEXICO
Archaeologists discovered that the famed Kukulcán pyramid at Chichén Itzá is made up of three pyramids nested within one another. They theorize the structure was built in three phases: the innermost pyramid during the years A.D. 550–800, the middle layer in 800–1000 and the outermost layer in 1050–1300.

INDONESIA
Particulate pollution from a string of wildfires in 2015 may have led to as many as 17,270 premature deaths from respiratory illness across Southeast Asia, according to a new report. The fires were intentionally set to clear land but grew out of control and burned through at least 6.4 million acres. They most likely were exacerbated by drier than usual El Niño weather.

SPAIN
Scientists in the Canary Islands had to halt research projects for two months while waiting for a shipment of 29 transgenic mice. Commercial airlines to the islands had decided to stop transporting laboratory animals, citing safety concerns. A military plane eventually delivered the goods.

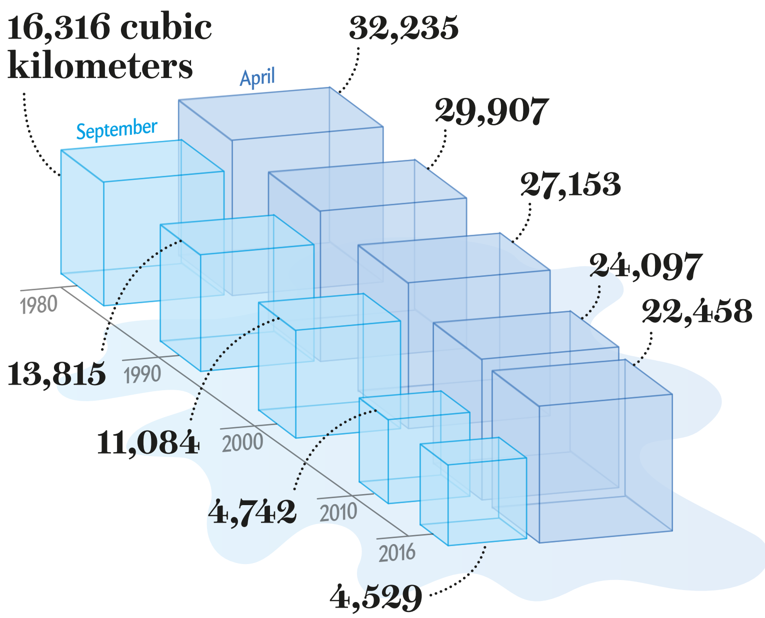
For more details, visit www.ScientificAmerican.com/feb2017/advances

CLIMATE CHANGE

Icy Retreat

The extent of ice loss at the top of the world, as seen by satellites, is literally the tip of the iceberg. Although the Arctic ice cap's shrinkage is often expressed in terms of area, the change in volume is just as striking. Between 1980 and 2016 the amount of summer ice in cubic kilometers has decreased by an estimated 72 percent. The numbers for 2016 only buttressed the trend: ice hit record lows for the months of October and November. The Arctic may be free of ice by midcentury if we continue emitting greenhouse gases at the current rate, says Julienne Stroeve, a researcher at the U.S. National Snow and Ice Data Center.

—*Ryan F. Mandelbaum*



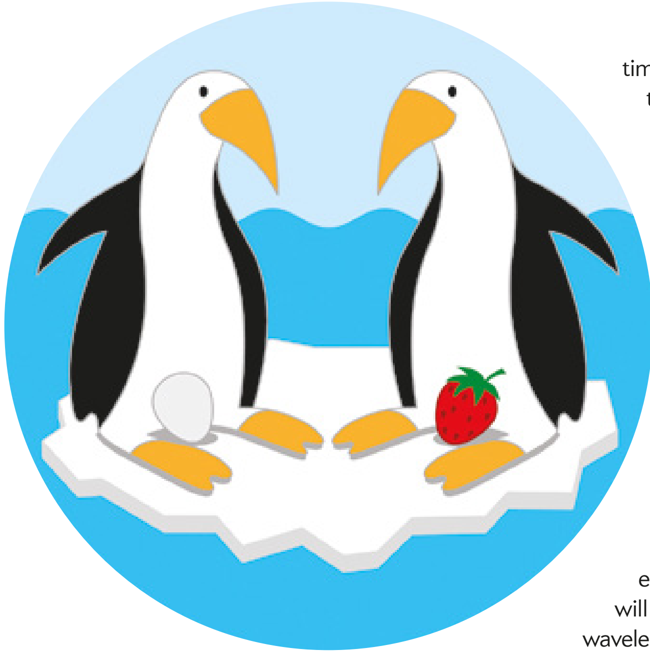
SOURCE: PIOMAS MONTHLY ICE VOLUME DATA, 1979–PRESENT, POLAR SCIENCE CENTER, UNIVERSITY OF WASHINGTON *http://psc.apl.uw.edu/research/projects/arctic-sea-ice-volume-anomaly/data*

Graphic by Amanda Montañez

ENGINEERING

Fruits for the Frozen

A new Antarctic-proof greenhouse heads south to polar scientists



In the endless winter that is Antarctica, the picture of decadence is a juicy strawberry. Research scientists at the Neumayer III polar station may soon be so lucky as to count the treat—and other fresh fruits and vegetables—as part of their diets: engineers at the German Aerospace Center are currently building them a year-round greenhouse.

Called Eden ISS, the closed-system, 20-foot-long shipping container will head to Antarctica in October. The project is now in its final phase; next month Paul Zabel, the future caretaker of the greenhouse, and his colleagues will begin a trial of the garden in Bremen. In simulated Antarctic isolation, they plan to grow between 30 and 50 different species, including tomatoes, peppers, lettuce and strawberries, as well as herbs such as basil and parsley that could add fresh flavors to the packaged foods that make up the typical diet of an Antarctic scientist. "We are focused on pick-and-eat crops—plants that don't need any post-processing," Zabel says.

Cultivating greens in the Antarctic's hostile conditions requires extreme measures—temperatures on the Ekström Ice Shelf can drop to –22 degrees Fahrenheit, and the sun disappears for months at a time. To beat the odds, Zabel has turned to the growing method known as aeroponics, which eliminates the need for soil (greenhouses at the American and Australian stations use this method, too). Instead fruit and veggie plants will sit on racks with their roots hanging in the air, where they receive a spritz of nutrient-rich mist every few minutes. Extra carbon dioxide will be pumped into the 75-degree F greenhouse for enrichment, and 42 LED lamps will be tuned to the red and blue wavelengths that plants thrive on, giving the greenhouse a purplish glow.

Biting into a ripe fruit or vegetable could boost morale for the 10 crew members set to overwinter at Neumayer III next season. But the garden is more than a treat for polar scientists, Zabel says. Ultimately the project is designed to test techniques for efficiently cultivating plant-based food in even more extreme environments, such as on the International Space Station or Mars.

—Megan Gannon

Atlantic bluefin tuna

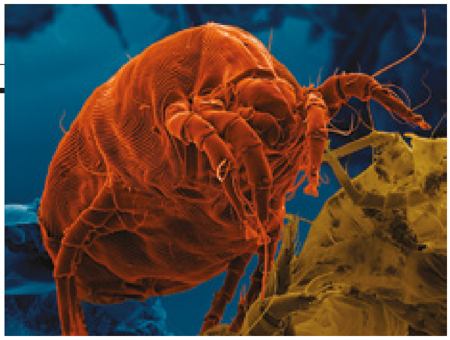
ENVIRONMENT

"[This] tells me we don't just have to wring our hands about the high level of mercury in these fish. There is something we can do about it and get pretty quick results."

—Nicholas Fisher, a marine biogeochemist at Stony Brook University and co-author of a recent study that found mercury levels in Atlantic bluefin tuna decreased by 19 percent between 2004 and 2012. Fisher and his colleagues directly linked the decline to reduced mercury emissions in North America—most of which is attributable to an industry shift away from coal.

GETTY IMAGES

Illustration by Thomas Fuchs



BOB SACHA *Getty Images*

HEALTH

Go West, Allergy Sufferers

Dust mites don't like the arid regions of the U.S.

It's possible to escape some tree and weed allergies by moving to a new town, state or region, and the same may be true of dust-mite allergies. The microscopic arachnids—which leave behind feces and corpses that can trigger allergic responses and asthma—are sparse across large swaths of the Great Plains and Mountain West, according to a new survey of the arthropods that inhabit our homes.

With the help of citizen scientists, researchers from North Carolina State University and the University of Colorado Boulder analyzed arthropod DNA found in 732 dust samples collected from interior door frames throughout the U.S. Amid their data on many other species, the scientists found that the eastern U.S. and the West Coast are dust-mite utopias, whereas much of the western interior may be a comparative desert. Why? Because mites need high humidity to survive. (They cannot drink; instead they absorb moisture from the air to stay hydrated.)

Lead author Anne Madden cautions that just because samples from parts of the West tested negative for dust mites, it does not mean those areas are devoid of the critters. Even in dry regions, mattresses and carpets—as well as furniture moved from humid areas—may harbor dust-mite colonies, says David Miller, who studies the links between damp housing and health at Carleton University in Ottawa and was not involved in this study.

An estimated 20 million Americans suffer from allergies to these tiny creatures. "If you're allergic to dust mites, living in dry-land America and Canada and in high elevations is absolutely a good thing," Miller says. But you don't have to move across the country to escape: encasing mattresses and pillows in allergen-proof covers, laundering sheets once a week and vacuuming frequently with a machine fitted with a HEPA filter will help banish the bugs. —*Jennifer Frazer*

Increasingly militaristic antipoaching efforts in Africa often put rangers in risky or even life-threatening situations.

Q&A

The Trauma of Saving Animals

A clinical psychologist treats shell-shocked rangers engaged in Africa's poaching wars

Poachers across Africa killed more than 24,000 elephants and 1,300 rhinos in 2015 alone—but animals are not the only victims of the illegal wildlife trade. An estimated 1,000 rangers have been killed in the line of duty over the past decade, and that figure will likely grow: 82 percent of the 570 rangers the World Wildlife Fund recently surveyed in 12 African countries said that they have faced life-threatening circumstances. The so-called war on poaching also takes a psychological toll—one that experts are only beginning to recognize. Susanna Fincham, a clinical psychologist in Sabie, South Africa, is one of the first to investigate the mental health issues plaguing rangers—and to devise ways of treating them. She recently spoke with Scientific American about the particular challenges she sees. Edited excerpts follow. *—Rachel Nuwer*

Scientific American: Why are rangers especially prone to developing anxiety, depression and post-traumatic stress disorder?
Susanna Fincham: Rangers are trained to conserve wildlife, and in the past firearm use was limited to controlling trouble animals. But starting around 2006, poaching began escalating to the point that rangers now must aim their firearms at other humans. In Kruger National Park—one of the places where I work—there are daily insurgencies by poaching cartels that are structured, organized and well equipped. It's a case of guerilla warfare, and danger is extremely high. As a result, rangers are exposed to a great deal of trauma.

How do you mitigate those issues?
I use counseling techniques to try to help rangers avoid becoming victims of PTSD. This entails careful clinical assessment of their emotional state. One step is psychoeducation, or the impartment of knowledge about the body's response to trauma, including why they sweat, shake, struggle to fall asleep and have increased startle reflexes. I train them to feel less stressed by controlling their breathing and muscle tension. I also take a narrative approach, asking them, for example, to tell me a story about the worst thing that has happened to them. I ask how that made them feel and then point out that these stressful symptoms are normal and that they survived the incident. To deliver anxiety relief, you have to get them to understand that they are actually alive, that they have come through.

Are there many psychologists performing similar services?
No, not at all. Previously people focused more on the soldier role of rangers rather than on their well-being. The need is only now being recognized. There's also still strong stigma in South Africa of seeing a psychologist, especially for men. But now more senior rangers are seeking assistance, so we're chipping away at that wall. I've seen approximately 120 rangers since 2011, and I also speak with family members about their concerns. There are as many as 25,000 rangers throughout Africa.

What is next for you and the rangers?
I'm developing a culturally sensitive therapeutic strategy specifically for rangers, and I'd like to collate and publish all the information I've found so it's available for anyone who wants to use it. Long term, I would also love to see a special independent unit of psychologists and social workers established for rangers.

CLOCKWISE: TONY KARUMBA *Getty Images*; GETTY IMAGES; MICHAEL GOTTSCHALK *Getty Images*

Stomach Upset

Doctors and patients are grappling with the unsettling finding that chronic use of popular heartburn medicines may be riskier than was thought

By Karen Weintraub

Over-the-counter packages of Nexium, Prevacid and Prilosec tell you to take the pills—known to doctors as proton-pump inhibitors, or PPIs—for just two weeks at a time unless otherwise directed by a physician. Yet drugs of this best-selling class prevent heartburn and ease related ailments so well that patients—particularly those who suffer from a condition called GERD (gastroesophageal reflux disease)—are often advised to take the medications for years. By decreasing acid production in the stomach, the agents prevent the caustic liquid from backing up—or refluxing—into the esophagus, where it can cause pain and can damage the food tube's delicate lining.

In recent years, though, safety questions have been raised about prolonged use of the blockbuster drugs. (The medications appear to be safe when taken for a short period, as directed.) Some studies, for example, have linked continuous treatment with proton-pump inhibitors to serious infections caused by the bacterium *Clostridium difficile.* Presumably something about lowering the acid environment of the stomach allows the pathogens to survive when they otherwise might not. Other investigations suggest long-term changes in the stomach's acid content can lead to improper absorption of several vitamins—such as B12—and minerals, triggering bone loss, among other ill effects.

Perhaps the biggest surprise came last year when two studies linked the regular use of proton-pump inhibitors to conditions that were seemingly unrelated to the acid levels of the stomach. One of the studies, published in *JAMA Neurology,* found that the drugs increased the risk of developing dementia, including Alzheimer's disease; the other, published in *JAMA Internal Medicine,* suggested a greater risk of kidney problems.

The papers did not prove that PPIs cause the problems. But some researchers have nonetheless suggested possible mechanisms by which long-term use of the drugs could trigger dementia or kidney problems. A reduction in vitamin B12, for example, might leave the brain more vulnerable to damage, says Britta Haenisch, an author of the *JAMA Neurology* study and a neuropharmacologist at the Bonn campus of the German Center for Neurodegenerative Diseases. Last spring clinicians at the Houston Methodist Research Institute reported another plausible explanation for how PPIs might lead to these unexpected health issues: they picked up signs that the drugs act not only in the stomach but elsewhere in the body, too.

These discoveries leave patients and doctors alike wondering who should and should not use proton-pump inhibitors long term. "At this point, we don't have enough data to weigh one risk versus the other," says Kyle Staller, a leading gastroenterologist at Massachusetts General Hospital. But he and others are feeling their way forward.

PROTON PUMPS

SOME AMOUNT OF ACID IS, of course, crucial for the stomach to break down food. Specialized cells that dot the stomach's inner lining pump out hydrogen ions, or protons, which, from a chemical point of view, are what make the stomach's juices so acidic. As the name implies, proton-pump inhibitors reduce acid in the stomach—and thus reflux into the esophagus—by shutting down many of these cellular pumps. The shutdown is permanent, but the drugs are not cures, because the cells re-

Illustration by Augusto Zambonato

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place lost pumps. Another popular class of drugs known as H2 blockers (Tagamet among them) also limit acid production but in a different, less powerful way. Antacids, such as Tums, neutralize stomach acids but are even less potent, useful only for occasional, mild discomfort.

The effectiveness of PPIs has fueled a huge surge in their use since their release in the 1980s. Today they are available both over the counter and by prescription, and Nexium remains one of the most prescribed medications in the world.

The studies reported in 2016 grew out of earlier hints that such chronic use could affect the brain and kidneys. One 2013 study in *PLOS ONE,* for instance, found that proton-pump inhibitors can enhance the production of beta-amyloid proteins, a hallmark of Alzheimer's. Three years later the *JAMA Neurology* study, which included 74,000 Germans older than 75, found that regular PPI users had a 44 percent higher risk of dementia than those not taking PPIs.

Similarly, worries about kidneys emerged from evidence that people with sudden renal damage were more likely to be taking PPIs. In one 2013 study in *BMC Nephrology,* for example, patients with a diagnosis of kidney disease were found to be twice as likely as the general population to have been prescribed a PPI. The 2016 study of PPIs and kidney disease, which followed 10,482 participants from the 1990s through 2011, showed that those who took the drug suffered a 20 to 50 percent higher risk of chronic kidney disease than those who did not. And anyone who took a double dose of PPIs every day had a much higher risk than study subjects who took a single dose.

The 2016 Houston Methodist study that suggests a new explanation for a link between PPIs and Alzheimer's or kidney problems looked at cells that were grown in culture. It showed that besides acting on cells in the stomach, the drugs also affect certain cells that normally line blood vessels.

As with many other cells in the body, those in blood vessel walls need to make acid so that they can break down and get rid of abnormal or damaged proteins. The cells safely store the acid in special internal compartments, which essentially serve as molecular garbage dumps. If, however, a cell's internal trash is not broken down—as occurs if acid levels are too low—bits of microscopic detritus start to pile up. A cell overflowing with its own garbage cannot function properly and quickly becomes damaged. "We actually showed these rubbish piles accumulating in the cells," says John Cooke, a cardiovascular researcher at Houston Methodist and one of the study authors. The resulting problems can become particularly severe wherever many blood vessels are found—as is the case in the brain and kidneys. Indeed, some recent studies have also hinted at a possible connection between long-term use of PPIs and damage to another organ with lots of blood vessels, the heart.

Though reasonable, Cooke's conclusion cannot be considered proved. Proof would require more study of the effect of proton-pump inhibitors on the vasculature in animals or humans, as opposed to cell cultures. Researchers also need to explore other factors that could account for the link between PPIs and dementia, heart disease or kidney problems. After all, some of the most well-known risks for these conditions are smoking, obesity and a high-fat diet, which, as it happens, also increase the likelihood of acid reflux. In this case, use of drugs could be a marker for certain unhealthy habits—versus a new, additional cause for these conditions.

DECISIONS, DECISIONS

WITHOUT CONCLUSIVE DATA, physicians and patients have to balance the need to prevent the ill effects of excess stomach acid and reflux with the desire to avoid potentially serious—if theoretical—side effects from long-term use of PPIs.

Many doctors worry that reports of potential side effects will scare away patients who have a real need for the medication. Some people with GERD, for example, suffer from such miserable heartburn without PPIs that they struggle with daily life. Untreated acid reflux also carries risks besides acute pain. Studies have shown that it may, over time, alter the lining of the esophagus in a way that increases the risk for a condition called Barrett's esophagus, which can, in turn, be a precursor to cancer. Reducing acid is thought to help reduce the risk. (It is also possible to get Barrett's esophagus or cancer without having had any reflux symptoms, however.)

Gather and evaluate as much information as possible—and be prepared to change course.

Whenever one of Staller's patients at Mass General says he or she wants to stop taking a PPI, he likes to perform a simple test. He has the person stop taking the medication for a week and substitutes Tagamet or another H2 blocker. (Stopping a PPI cold turkey, without adding another drug, typically causes a rebound effect, pushing the stomach to produce even more acid than it otherwise would.) He also recommends cutting back on acidic and spicy food for the length of the test. Then he sees if the patient is still bothered by heartburn at the end of a week, especially during the day, when gravity should help prevent acid from rising up into the throat. The persistence of heartburn indicates the presence of a more severe problem, Staller says. And thus, the benefit of taking a daily PPI outweighs the risks in such cases.

The calculus, obviously, is different for everyone. For Vicki Scott Burns, a children's book author in Bolton, Mass., PPIs are "the lesser of two evils." She says her quality of life is vastly better on the drugs. Others might reach an alternative conclusion. In the end, Staller and other health experts advise patients and their physicians to gather and evaluate as much information as possible before making a decision—and to be prepared to change course if new evidence comes to light. SA

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

How to Stamp Out Fake News

New algorithms will help—but users' skepticism is the ultimate weapon

By David Pogue

"Pope Francis Shocks World, Endorses Donald Trump for President." "FBI Agent Suspected in Hillary Email Leaks Found Dead of Apparent Murder-Suicide." "Rush Reveals Michelle's Perverted Past After She Dumps on Trump." Those headlines didn't come from the *New York Times* or CNN; they were likely written by teenagers in Macedonia. Those fake news stories were written as clickbait, designed to draw readers to fake-news sites, where the Balkan teens made money by selling ads.

If last fall's election will go down in history as the Election of Unintended Consequences, those fake stories are no exception. They wound up circulating copiously on Twitter and Facebook; on the latter, the top-20 fake stories actually triggered more clicks than the top-20 real ones. Fake news became fodder for ugly partisan warfare online, too. Worst of all, it might have affected the presidential election results. Remember, 44 percent of U.S. adults get their news from Facebook.

You wouldn't think that fake news would be controversial. Surely we all agree that something as important as a presidential election should be based on truth. Can't we just ask Facebook and Twitter to block fake news?

We can, but they can't. The problem isn't technological—it's philosophical. "Identifying the 'truth' is complicated," Facebook CEO Mark Zuckerberg wrote in response to the phenomenon of fake news. "While some hoaxes can be completely debunked, a greater amount of content, including from mainstream sources, often gets the basic idea right but some details wrong or omitted. An even greater volume of stories express opinions that many will disagree with and flag as incorrect even when factual."

So yes, the headline about the pope was clearly fake. But what about rumor and gossip stories? How can anyone know if they're true? Or what about satire stories from, for example, the Onion and the *New Yorker*'s Andy Borowitz? Neither makes any attempt to deceive, and yet both are often passed around online as fact by people who suffer from, ahem, humor-deficit disorder.

Once fake news became a headline, both Google and Facebook stopped accepting advertising relationships with fake-news sites. There goes the financial incentive of those Macedonian teenagers.

And despite Zuckerberg's initial assertion that it's "extremely unlikely hoaxes changed the outcome of this election," Facebook is taking more steps to fight the problem—by making it easier to report fake stories, for example, and considering the addition of warning labels to stories that readers have flagged as phony.

But here's the thing. Remember the first time it became possible to assemble customized news pages (like Google News), where you saw news stories pertaining to your interests and nothing more? People worried that we'd never be exposed to stories that we might have stumbled onto when flipping, say, through a newspaper.

Well, the Facebook problem is a thousand times worse. On social media sites, *you* decide whose posts you want to read. On Facebook, they're your friends; on Twitter, they're people you choose to follow. In both cases, you're following like-minded people, whose opinions you prefer. In other words, you're no longer choosing *topics* you want to read about; now you're choosing which *slant* on the news you want to see. You're building your own echo chamber.

All of this helps explain why the "let the community decide" approach to filtering out bogus stories is problematic. For everyone in your echo chamber who flags a story as fake, the parallel universe on the other side of the hyperpartisan divide will mark it as true.

If we ever decide to do this presidential election thing again, the fake news stories will still be around. But three things will be different, all hopeful signs. First, Facebook and Google will have removed the ad-revenue incentive for publishing them. Second, Facebook's planned new policies and algorithms will, at least, screen out some of the deliberately misleading stories.

Above all, we'll be more cynical. Having lived through the first major fake-news election cycle and then spent four years talking about it, maybe we'll be more discerning next time. SA

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Illustration by Thomas Fuchs

The

Exercise *Paradox*

EVOLUTION

Studies of how the human engine burns calories help to explain why physical activity does little to control weight—and how our species acquired some of its most distinctive traits

By Herman Pontzer

Illustration by Bomboland

IN BRIEF

Conventional wisdom holds that physically active people burn more calories than less active people do.

But studies show that traditional hunter-gatherers, who lead physically hard lives, burn the same number of calories as people with access to modern conveniences.

The discovery that human energy expenditure is tightly constrained raises questions about how our large brain and other energetically demanding traits evolved.

Comparisons with energy expenditure in great apes suggest that the human metabolic engine has evolved to get more work done to support our costly features.

Herman Pontzer is an anthropologist at Hunter College. He studies energy expenditure in humans and great apes to test hypotheses about the evolution of human physiology and anatomy.

Still no giraffe. Four of us had been walking half the day, tracking a wounded giraffe that Mwasad, a Hadza man in his late 30s, shot the evening before. He hit it in the base of the neck from about 25 yards with a steel-tipped, wood arrow smeared with powerful, homemade poison. Hadza are traditional hunter-gatherers who live off of wild plants and animals in the dry savanna wilderness of northern Tanzania. They know the landscape and its residents better than you know your local Trader Joe's. Mwasad had let the giraffe run to give the poison time to work, hoping to find it dead in the morning. An animal that size would feed his family and his camp for a week—but only if he could locate it.

Mwasad led our party—Dave Raichlen from the University of Arizona, a 12-year-old Hadza boy named Neje and me—out of camp just after daybreak. Dave and I were of little use in this endeavor. Mwasad had invited us along as a friendly gesture and for the extra help to carry the butchered animal back to camp should our search effort succeed. As anthropologists who study human ecology and evolution, we jumped at the opportunity to tag along—Hadza men's tracking abilities are legendary. It certainly beat the prospect of a long day in camp spent fiddling with research equipment.

We walked hard for an hour through a pathless, rolling sea of golden, waist-high grass, dotted with brush and thorny acacia trees, directly to the bloody patch where the giraffe was struck. That bit of navigation in itself was quite a trick, like someone leading you to the middle of a 1,000-acre wheat field to show you where he had once dropped a toothpick and then nonchalantly reaching down to pick it up. Hour on hour, tracking the wounded animal under a relentless sun ensued as we followed ever more tenuous signs.

Still no giraffe. At least I had water. We sat in the shade of some bushes just after midday, taking a break while Mwasad pondered where the injured creature might head. I had a quart or so left—enough, I figured, to get through the heat of the afternoon. Mwasad, however, had not brought any water with him, as is typical of the Hadza. As we packed up to restart the search, I offered him a drink. Mwasad gave me a sideways look, smiled and proceeded to drink the entire bottle in one long pull. When he finished, he casually handed me the empty bottle.

It was karma. Dave and I, along with anthropologist Brian Wood from Yale University, had spent the past month living with the Hadza, conducting the first direct measurements of daily energy expenditure in a hunter-gatherer population. We enlisted a couple of dozen Hadza women and men, Mwasad among them, to drink small, incredibly expensive bottles of water enriched in two rare isotopes, deuterium and oxygen 18. Analyzing the concentration of those isotopes in urine samples from each participant would allow us to calculate their body's daily rate of carbon dioxide production and thus their daily energy expenditure. This approach, known as the doubly labeled water method, is the gold standard in public health for measuring the calories burned each day during normal daily life. It is straightforward, completely safe and accurate, but it requires that participants drink every last drop of the enriched water. We had taken pains to make clear that they must not spill, that they had to finish the dose completely. Mwasad seemed to have taken that message to heart.

Mwasad's sly joking aside, my colleagues and I have learned a lot about how the human body burns calories through our work with the Hadza. Together with findings from investigators who study other populations, our research has revealed some surprising insights into human metabolism. Our data indicate that, contrary to received wisdom, humans tend to burn the same number of calories regardless of how physically active they are. Yet we have evolved to burn considerably more calories than our primate cousins do. These results help to explain two puzzles that might seem disparate at first but are, in fact, related: first, why exercise generally fails to aid weight loss and, second, how some of humanity's unique traits arose.

THE CALORIE ECONOMY

RESEARCHERS WHO ARE INTERESTED in human evolution and ecology often focus on energy expenditure because energy is central to everything in biology. One can learn a lot about any species by measuring its metabolism: life is essentially a game of turning energy into kids, and every trait is tuned by natural selection to maximize the evolutionary return on each calorie spent. Ideally, the study population lives in the same environments in which the species originally evolved, where the same ecological pressures that shaped its biology are still at work. That is difficult to achieve with human subjects because most people are divorced from the daily work of acquiring food from a wild landscape. For nearly all the past two million years, humans and our ancestors have been living and evolving as hunter-gatherers. Farming only got going about 10,000 years ago; industrialized cities and modern technology are only a few generations old. Populations such as the Hadza, one of the last hunter-gatherer populations left in the world, are key to understanding how our bodies evolved and functioned before cows, cars and computers.

Life for the Hadza is physically demanding. Each morning the women leave the grass huts of camp in small groups, some carrying infants on their back in a wrap, foraging for wild berries or other edibles. Wild tubers are a staple of the Hadza diet, and women can spend hours digging them out of the rocky ground with sticks. Men cover miles each day hunting with bows and arrows they make themselves. When game is scarce, they use simple hatchets to chop into tree limbs, often 40 feet up in the canopy, to harvest wild honey. Even the children contribute, hauling buckets of water back from the nearest watering hole, sometimes a mile or more from camp. In the late afternoon, folks wend their way back to camp, sitting on the ground and talking around small cooking fires, sharing the day's returns and tending to the kids. Days roll along like this through dry and wet seasons, ad millennium.

But forget any romantic notions of some lost Eden. Hunting and gathering is cerebral and risky, a high-stakes game in which the currency is calories and going bust means death. Men such as Mwasad spend hundreds of calories a day hunting and tracking, a gamble that they hope will pay off in game. Savvy is just as critical as stamina. Whereas other predators can rely on their speed and strength to obtain prey, humans have to outthink their quarry, considering their behavioral tendencies and scouring the landscape for signs of game. Still, Hadza men land big game like giraffes only about once a month. They would starve if Hadza women were not executing an equally sophisticated, complementary strategy, using their encyclopedic knowledge of local plant life to bring home a reliable bounty every day. This complex, cooperative foraging is what made humans so incredibly successful and is the core of what makes us unique.

Researchers in public health and human evolution have long assumed that our hunter-gatherer ancestors burned more calories than people in cities and towns do today. Given how physically hard folks such as the Hadza work, it seems impossible to imagine otherwise. Many in public health go so far as to argue that this reduction in daily energy expenditure is behind the global obesity pandemic in the developed world, with all those unburned calories slowly accumulating as fat. One of our motivations for measuring Hadza metabolism was to determine the size of this energy shortfall and see just how deficient we Westerners were in our daily expenditure. Back home in the U.S. after a hot and dusty field season, I lovingly packed the vials of Hadza urine on dry ice and sent them away to the Baylor College of Medicine, home of one of the best doubly labeled water laboratories in the country, imagining the whopping calorie totals they would reveal.

But a funny thing happened on the way to the isotope ratio mass spectrometer. When the analyses came back from Baylor, the Hadza looked like everyone else. Hadza men ate and burned about 2,600 calories a day, Hadza women about 1,900 calories a day—the same as adults in the U.S. or Europe. We looked at the data every way imaginable, accounting for effects of body size, fat percentage, age and sex. No difference. How was it possible? What were we missing? What else were we getting wrong about human biology and evolution?

LIES MY FITBIT TOLD ME

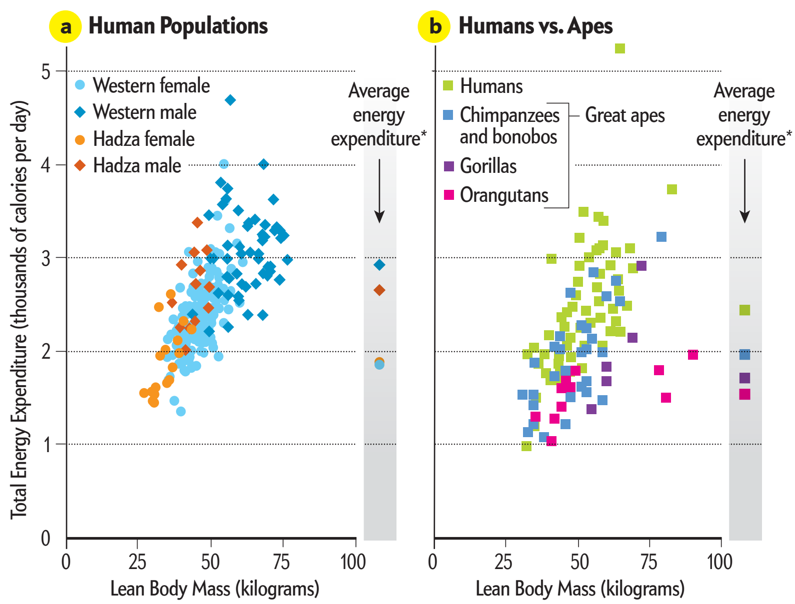
IT SEEMS SO OBVIOUS and inescapable that physically active people burn more calories that we accept this paradigm without much critical reflection or experimental evidence. But since the 1980s and 1990s, with the advent of the doubly labeled water method, the empirical data have often challenged the conventional wisdom in public health and nutrition. The Hadza result, strange as it seemed, was not some thunderbolt from the blue but more like the first cold drop of water down your neck from a rain that had been building, ignored, for years.

The earliest doubly labeled water studies among traditional farmers in Guatemala, the Gambia and Bolivia showed their energy expenditures were broadly similar to those of city dwell-

FINDINGS

Gas Guzzlers

Experts have assumed that physically active people burn more calories than less active folks. But direct measurements of energy expenditure in modern-day hunter-gatherers in the developing world and comparatively sedentary populations in the U.S. and Europe reveal similar results **a**. If human metabolism is so tightly constrained, how did our big brain, long life span and other energetically costly features that distinguish us from our primate relatives evolve? Humans consume and expend hundreds of calories a day more than great apes **b**, suggesting that our metabolic engine changed to burn energy faster, thus powering our expensive traits.



*To account for differences in energy expenditure arising from body size, Western averages are calculated at Hadza body sizes, and great ape averages are calculated at average human body size.

SOURCES: "HUNTER-GATHERER ENERGETICS AND HUMAN OBESITY," BY HERMAN PONTZER ET AL., IN *PLOS ONE*, VOL. 7, NO. 7, ARTICLE NO. E40503; JULY 25, 2012 (*left*); "METABOLIC ACCELERATION AND THE EVOLUTION OF HUMAN BRAIN SIZE AND LIFE HISTORY," BY HERMAN PONTZER ET AL., IN *NATURE*, VOL. 533; MAY 19, 2016 (*right*)

Graphic by Jen Christiansen

ers. In a study published in 2008, Amy Luke, a researcher in public health at Loyola University Chicago, took this work a step further, comparing energy expenditure and physical activity in rural Nigerian women with that in African-American women in Chicago. Like the Hadza study, hers found no differences in daily energy expenditure between populations, despite large differences in activity levels. Following up on that work, Lara Dugas, also at Loyola, along with Luke and others, analyzed data from 98 studies around the globe and showed that populations coddled by the modern conveniences of the developed world have similar energy expenditures to those in less developed countries, with more physically demanding lives.

Humans are not the only species with a fixed rate of energy expenditure. On the heels of the Hadza study, I piloted a large collaborative effort to measure daily energy expenditure among primates, the group of mammals that includes monkeys, apes, lemurs and us. We found that captive primates living in labs and zoos expend the same number of calories each day as those in the wild, despite obvious differences in physical activity. In 2013 Australian researchers found similar energy expenditures in sheep and kangaroos kept penned or allowed to roam free. And in 2015 a Chinese team reported similar energy expenditures for giant pandas in zoos and in the wild.

HADZA HUNTER-GATHERERS in Tanzania spend hundreds of calories a day on activity yet burn the same total number of calories as city dwellers in the U.S.

HARRY HOOK *Getty Images*

For a more granular look, comparing individuals instead of population averages, I recently joined Luke and her team, including Dugas, to examine activity and energy expenditure in a large, multiyear analysis known as the Modeling the Epidemiological Transition Study (METS). More than 300 participants wore accelerometers similar to a Fitbit or other fitness tracker 24 hours a day for an entire week while their daily energy expenditure was measured with doubly labeled water. We found that daily physical activity, tracked by the accelerometers, was only weakly related to metabolism. On average, couch potatoes tended to spend about 200 fewer calories each day than people who were moderately active: the kind of folks who get some exercise during the week and make a point to take the stairs. But more important, energy expenditure plateaued at higher activity levels: people with the most intensely active daily lives burned the same number of calories each day as those with moderately active lives. The same phenomenon keeping Hadza energy expenditure in line with that of other populations was evident among individuals in the study.

How does the body adjust to higher activity levels to keep daily energy expenditure in check? How can the Hadza spend hundreds of calories a day on activity yet burn the same total number of calories a day as comparatively sedentary people in the U.S. and Europe? We are still not sure, but the cost of activity per se is not changing: we know, for example, that Hadza adults burn the same number of calories to walk a mile as Westerners do. It could be that people with high activity levels change their behavior in subtle ways that save energy, like sitting rather than standing or sleeping more soundly. But our analysis of the METS data suggests that although these behavioral changes might contribute, they are not sufficient to account for the constancy seen in daily energy expenditure.

Another intriguing possibility is that the body makes room for the cost of additional activity by reducing the calories spent on the many unseen tasks that take up most of our daily energy budget: the housekeeping work that our cells and organs do to keep us alive. Saving energy on these processes could make room in our daily energy budget, allowing us to spend more on physical activity without increasing total calories spent per day. For example, exercise often reduces inflammatory activity that the immune system mounts as well as levels of reproductive hormones such as estrogen. In lab animals, increased daily exercise has no effect on daily energy expenditure but instead results in fewer ovulatory cycles and slower tissue repair. And extremes may lead some animals to eat their own nursing infants. Humans and other creatures seem to have several evolved strategies for keeping daily energy expenditure constrained.

All of this evidence points toward obesity being a disease of gluttony rather than sloth. People gain weight when the calories they eat exceed the calories they expend. If daily energy expenditure has not changed over the course of human history, the primary culprit in the modern obesity pandemic must be the calories consumed. This should not be news. The old adage in public health is that "you can't outrun a bad diet," and experts know from personal experience and lots of data that just hitting the gym to lose weight is frustratingly ineffective. But the new science helps to explain why exercise is such a poor tool for weight loss. It is not that we are not trying hard enough. Our bodies have been plotting against us from the start.

You still have to exercise. This article is not a note from your mom excusing you from gym class. Exercise has tons of well-documented benefits, from increased heart and immune system health to improved brain function and healthier aging. In fact, I suspect that metabolic adaptation to activity is one of the reasons exercise keeps us healthy, diverting energy away from activities, such as inflammation, that have negative consequences if they go on too long. For example, chronic inflammation has been linked to cardiovascular disease and autoimmune disorders.

The foods we eat certainly affect our health, and exercise paired with dietary changes can help keep off unwanted pounds once a healthy weight has been reached, but evidence indicates that it is best to think of diet and exercise as different tools with

SCIENTIFIC AMERICAN ONLINE Learn more about the evolution of human metabolism at ScientificAmerican.com/feb2017/pontzer different strengths. Exercise to stay healthy and vital; focus on diet to look after your weight.

ENERGY BUDGETS AND EVOLUTION

EVEN AS THE RECENT SCIENCE in metabolic adaptation helps to clarify the relation between exercise and obesity, a constrained, adaptive metabolism leaves researchers with larger, existential questions. If daily energy expenditure is virtually immobile, how could humans evolve to be so radically different from our ape relatives? Nothing in life is free. Resources are limited, and investing more in one trait inevitably means investing less in another. It is no coincidence that rabbits reproduce prodigiously but die young; all that energy plowed into offspring means less for bodily maintenance and longevity. *Tyrannosaurus rex* can thank its big head of nasty teeth and powerful hind limbs for its puny arms and hands. Even dinosaurs couldn't have it all.

Humans flout this bedrock evolutionary principle of austerity. Our brains are so large that, as you sit reading this article, the oxygen from every fourth breath you take is needed just to feed your brain. Yet humans have bigger babies, reproduce more often, live longer and are more physically active than any of our ape relatives. Hadza camps are full of cheerfully chaotic children and hale, hearty men and women in their 60s and 70s. Our energetic extravagance presents an evolutionary puzzle. Humans are so genetically and biologically similar to other apes that researchers have long assumed that our metabolisms are similar, too. But if energy expenditures are as constrained as our Hadza study and others suggest, how could an inflexible, apelike metabolism process all the calories needed to support our costly human traits?

In the wake of our broad, comparative primate energetics study, my colleagues and I began to wonder whether humans' adaptive suite of energetically costly traits was fueled by a wholesale evolutionary change in metabolic physiology. We had found in that study that primates burn only half as many calories a day as other mammals do. The reduced metabolic rates of primates correspond with their slow rates of growth and reproduction. Perhaps, conversely, the faster reproduction and other expensive traits of humans were linked to the evolution of an increased metabolic rate. All that was needed to test this idea was getting a bunch of frenetic chimpanzees, wily bonobos, phlegmatic orangutans and skittish silverback gorillas to carefully drink doses of doubly labeled water without spilling and to provide a few urine samples. In a scientific tour de force, my colleagues Steve Ross and Mary Brown, both at Lincoln Park Zoo in Chicago, worked with caretakers and veterinarians from more than a dozen zoos across the U.S. to pull that off. It took a couple of years, but they accumulated enough data on great ape energy expenditure to provide a solid comparison with humans.

Sure enough, humans burn more calories each day than any of our great ape relatives. Even after accounting for effects of body size, activity level and other factors, humans consume and expend about 400 more calories a day than chimpanzees and bonobos do; differences with gorillas and orangutans are larger still. Those extra calories represent the extra work our bodies do to support larger brains, produce more babies and maintain our bodies so we live longer. It is not simply that we eat more than other apes (although we do that, too); as we know all too well, piling extra calories into a body that is not equipped to use them only results in obesity. Our bodies, right down to the cellular level, have evolved to burn energy faster and get more done than our ape relatives. Human evolution was not entirely without trade-offs: our digestive tract is smaller and less costly than other apes, which need a large, energetically expensive gut to digest their fibrous, plant-based diets. But the critical changes that make us human were fueled by an evolutionary shift in our metabolic engine.

SHARED FORTUNES

AT SOME POINT in the late afternoon, our path bent toward camp, Mwasad looking ahead instead of searching the ground. We were heading home sans giraffe. Here was the fundamental danger in the high-energy human strategy: coming home empty-handed was both more likely and more consequential. Many of the energy-rich foods we need to fuel our faster metabolisms are inherently difficult to obtain in the wild, increasing the energy cost of finding food and heightening the risk of starvation for the men and women out foraging and their kids back at camp.

Happily for Mwasad, humans have evolved a few tricks to keep starvation at bay. We are the only species that has learned to cook, which increases the caloric value of many foods and makes them more efficient to digest. Our mastery of fire converts otherwise inedible root vegetables—from Trader Joe's yams to wild Hadza tubers—into veritable starch bombs. We have also evolved to be fat. We know this all too well from the obesity crisis in the West, but even Hadza adults, lean by any human standard, carry twice as much fat as chimpanzees idling away in zoos. Problematic though it may be in our modern era, our propensity to store fat most likely coevolved with our faster metabolism as a critical energy buffer to survive lean times.

As the sun sat heavy and orange just above the trees, we melted back into camp, Dave and I toward our tents, Mwasad and Neje to their families' huts, each one of us glad to be home. Despite the lost giraffe, no one went hungry that evening. Instead, with little fanfare or conscious effort, the camp deployed our species' most ingenious and powerful weapon against starvation: sharing. Sharing food is so fundamental to the human experience, the common thread of every barbecue, birthday, bar mitzvah, that we take it for granted, but it is a unique and essential part of our evolutionary inheritance. Other apes do not share.

Beyond our nutritional requirements and fixation with fat, perhaps the most profound impact of our increased energy expenditure is this human imperative to work together. Evolving a faster metabolism bound our fortunes to one another, requiring that we cooperate or die. As I sat with Dave and Brian, recounting the day's adventures over tinned sardines and potato chips, I realized I would not have had it any other way. No giraffe, no problem. SA

MORE TO EXPLORE

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COSMOLOGY

POP *goes the universe*

THE LATEST ASTROPHYSICAL MEASUREMENTS, COMBINED WITH THEORETICAL PROBLEMS, CAST DOUBT ON THE LONG-CHERISHED INFLATIONARY THEORY OF THE EARLY COSMOS AND SUGGEST WE NEED NEW IDEAS

By Anna Ijjas, Paul J. Steinhardt and Abraham Loeb

Photographs by The Voorhes

ON MARCH 21, 2013, the European Space Agency held an international press conference to announce new results from a satellite called Planck. The spacecraft had mapped the cosmic microwave background (CMB) radiation, light emitted more than 13 billion years ago just after the big bang, in better detail than ever before. The new map, scientists told the audience of journalists, confirms a theory that cosmologists have held dear for 35 years: that the universe began with a bang followed by a brief period of hyperaccelerated expansion known as inflation. This expansion smoothed the universe to such an extent that, billions of years later, it remains nearly uniform all over space and in every direction and "flat," as opposed to curved like a sphere, except for tiny variations in the concentration of matter that account for the finely detailed hierarchy of stars, galaxies and galaxy clusters around us.

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The principal message of the press conference was that the Planck data perfectly fit the predictions of the simplest inflationary models, reinforcing the impression that the theory is firmly established. The book on cosmology seemed to be closed, the team suggested.

Following the announcement, the three of us discussed its ramifications at the Harvard-Smithsonian Center for Astrophysics. Ijjas was then a visiting graduate student from Germany; Steinhardt, who had been one of the original architects of inflationary theory three decades ago but whose later work pointed out serious problems with its theoretical foundations, was spending his sabbatical at Harvard; and Loeb was our host as chair of the astronomy department. We all remarked on the meticulously precise observations of the Planck team. We disagreed, however, with the interpretation. If anything, the Planck data disfavored the simplest inflation models and exacerbated long-standing foundational problems with the theory, providing new reasons to consider competing ideas about the origin and evolution of the universe.

In the years since, more precise data gathered by the Planck satellite and other instruments have made the case only stronger. Yet even now the cosmology community has not taken a cold, honest look at the big bang inflationary theory or paid significant attention to critics who question whether inflation happened. Rather cosmologists appear to accept at face value the proponents' assertion that we must believe the inflationary theory because it offers the only simple explanation of the observed features of the universe. But, as we will explain, the Planck data, added to theoretical problems, have shaken the foundations of this assertion.

FOLLOWING THE ORACLE

TO DEMONSTRATE inflation's problems, we will start by following the edict of its proponents: assume inflation to be true without question. Let us imagine that a professed oracle informed us that inflation definitely occurred shortly after the big bang. If we were to accept the oracle's claim as fact, what precisely would it tell us about the evolution of the universe? If inflation truly offered a simple explanation of the universe, you would expect the oracle's declaration to tell us a lot about what to expect in the Planck satellite data.

One thing it would tell us is that at some time shortly after the big bang there had to have been a tiny patch of space filled with an exotic form of energy that triggered a period of rapidly accelerated expansion ("inflation") of the patch. Most familiar forms of energy, such as that contained in matter and radiation, resist and slow the expansion of the universe because of gravitational self-attraction. Inflation requires that the universe be filled with a high density of energy that gravitationally self-repels, thereby enhancing the expansion and causing it to speed up. It is important to note, however, that this critical ingredient,

IN BRIEF

The latest measurements of the cosmic microwave background (CMB), the universe's oldest light, raise concerns about the inflationary theory of the cosmos—the idea that space expanded exponentially in the first moments of time.

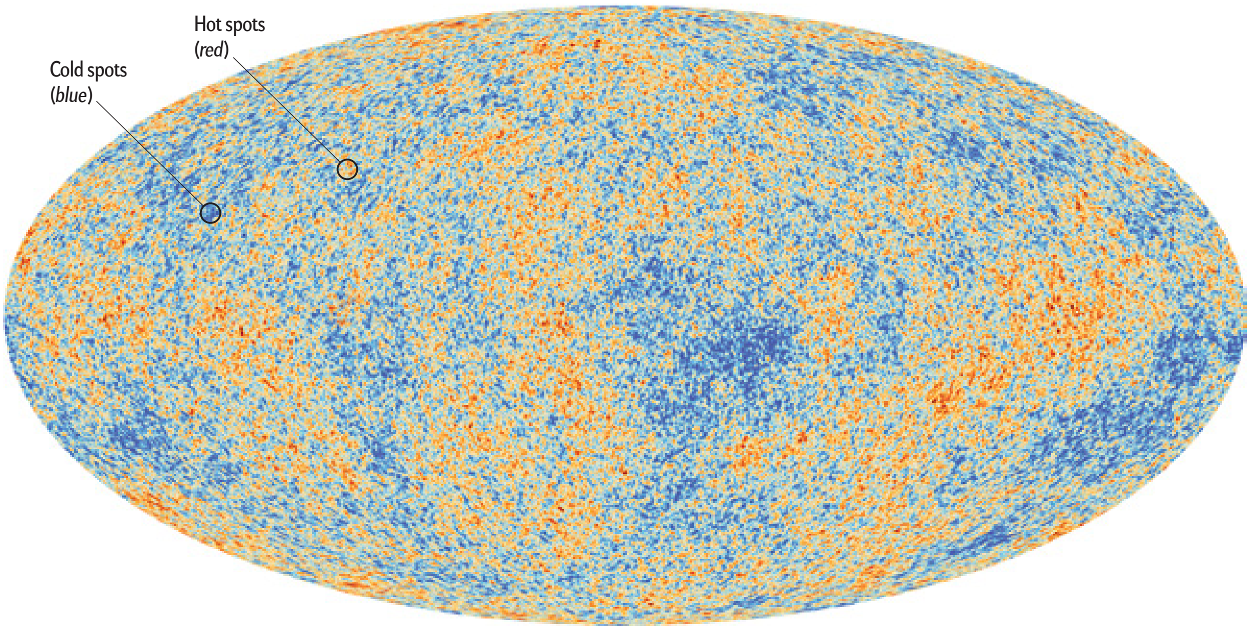
Inflation typically produces a different pattern of temperature variation in the CMB (although it can be made to predict almost any outcome). It would also generate primordial gravitational waves, which have not been found.

The data suggest cosmologists should reassess this favored paradigm and consider new ideas about how the universe began.

COSMOLOGICAL DATA

Snapshot of the Infant Universe

This map from the Planck satellite launched by the European Space Agency shows the cosmic microwave background (CMB)—the oldest observable light in the universe—which offers the best picture yet of the infant cosmos. Blue areas of the sky represent spots where the temperature of the CMB, and thus the early universe, was cooler, and red regions reflect warmer locales. Proponents of inflation, a theory suggesting the cosmos expanded rapidly in its first moments, claim that the pattern of hot and cold spots here is consistent with this notion. Yet the theory can actually produce any pattern and typically generates a larger variation in temperature than this map shows. Furthermore, if inflation took place the CMB should contain evidence of cosmic gravitational waves—ripples in spacetime caused by the early stretching—yet it does not. Instead the Planck data reveal that the real story of our universe's history is still wide open.



referred to as inflationary energy, is purely hypothetical; we have no direct evidence that it exists. Furthermore, there are literally hundreds of proposals from the past 35 years for what the inflationary energy may be, each generating very different rates of inflation and very different overall amounts of stretching. Thus, it is clear that inflation is not a precise theory but a highly flexible framework that encompasses many possibilities.

But what could the oracle's assertion tell us that is true for all the models, independent of the specific type of inflationary energy? For one thing, we could be sure from our basic knowledge of quantum physics that the temperature and density of matter throughout the universe after inflation ends must vary somewhat from place to place. Random quantum fluctuations in the concentration of inflationary energy on subatomic scales would be stretched during inflation into cosmic-sized regions with differing amounts of inflationary energy. According to the theory, the accelerated expansion ends when the inflationary energy decays into ordinary matter and radiation. In places where the inflationary energy density (the amount of inflationary energy in a cubic meter of space) is slightly greater, the accelerated expansion would last slightly longer, and the density and temperature of the universe would be slightly higher when the inflationary energy finally decays. The quantum-induced variations in inflationary energy would thereby be transcribed into a pattern of slightly hotter and colder spots in the cosmic microwave background light, which preserves a record of those times. Over the ensuing 13.7 billion years, the tiny density and temperature variations in the cosmos would condense under the influence of gravity to form a pattern of galaxies and large-scale structures.

That is a good start, though somewhat vague. Could we predict the numbers and arrangements of galaxies throughout space? The degree to which space is curved and warped? The amount of matter, or other forms of energy, that makes up the current universe? The answer is no. Inflation is such a flexible idea that any outcome is possible. Does inflation tell us why the big bang happened or how the initial patch of space was created that eventually evolved into the universe observed today? The answer, again, is no.

If we knew inflation to be true, we would also not be able to predict much about the hot and cold spots observed by the Planck satellite. The Planck map and earlier studies of the CMB indicate that the pattern of hot and cold spots is nearly the same no matter how close in you zoom, a property that scientists call "scale invariance." The latest Planck data show that the deviation from perfect scale invariance is tiny, only a few percent, and that the average temperature variation across all spots is rough-

COURTESY OF ESA AND PLANCK COLLABORATION ly 0.01 percent. Proponents of inflation often emphasize that it is possible to produce a pattern with these properties. Yet such statements leave out a key point: *inflation allows many other patterns of hot and cold spots that are not nearly scale-invariant and that typically have a temperature variation much greater than the observed value.* In other words, scale invariance is possible but so is a large deviation from scale invariance and everything in between, depending on the details of the inflationary energy density one assumes. Thus, the arrangement Planck saw cannot be taken as confirmation of inflation.

Notably, if we knew inflation had occurred, there is one feature we could be fairly certain of finding in the Planck CMB observations because it is common to all the simplest forms of inflationary energy, including those presented in standard textbooks. At the same time that quantum fluctuations produce random variations in inflationary energy, they also produce random warps in space that propagate as waves of spatial distortion across the universe once inflation ends. These disturbances, known as gravitational waves, are another source of hot and cold spots in the cosmic microwave background radiation, albeit ones that have a distinctive polarizing effect (that is, the gravitational waves cause light to have a certain preferred orientation for its electric field, depending on whether the light comes from a hot or cold spot, or some place in between).

The simplest inflationary models, including those described in standard textbooks, are strongly disfavored by observations. Of course, theorists rapidly rushed to patch the inflationary picture but at the cost of making arcane models.

Unfortunately, the search for inflationary gravitational waves has not panned out. Although cosmologists first observed hot and cold spots with the COBE (COsmic Background Explorer) satellite in 1992 and with many subsequent experiments, including even more recent Planck satellite results from 2015, they have not found any signs of the cosmic gravitational waves expected from inflation, as of this writing, despite painstaking searches for them. (On March 17, 2014, scientists at the BICEP2 experiment at the South Pole announced the detection of cosmic gravitational waves but later retracted their claim when they realized they had actually observed a polarization effect caused by dust grains within the Milky Way.) Note that these expected cosmic gravitational waves have nothing to do with the gravitational waves created by merging black holes in the modern universe found by the Laser Interferometer Gravitational wave Observatory (LIGO) in 2015.

The Planck satellite results—a combination of an unexpectedly small (few percent) deviation from perfect scale invariance in the pattern of hot and colds spots in the CMB and the failure to detect cosmic gravitational waves—are stunning. For the first time in more than 30 years, the simplest inflationary models, including those described in standard textbooks, are strongly disfavored by observations. Of course, theorists rapidly rushed to patch the inflationary picture but at the cost of making arcane models of inflationary energy and revealing yet further problems.

A SKIER ON A HILL

To fully appreciate the impact of the Planck measurements, it helps to take a close look at the inflationary models that proponents of inflation are putting forward, warts and all.

Inflationary energy is thought to arise from a hypothetical field, called the inflaton, analogous to an electric field, that permeates space and has a strength (or value) at every point in space. Because the inflaton is hypothetical, theorists are free to imagine that the inflaton is gravitationally self-repulsive to cause the expansion of the universe to accelerate. The strength of the inflaton field at a given point in space determines the inflationary energy density there. The relation between the strength of the field and the energy density can be represented by a curve on a graph that looks like a hill [*see box on opposite page*]. Each of the hundreds of inflationary energy models that have been proposed has a precise shape for this hill that determines the properties of the universe after inflation is over—for instance, whether or not the universe is flat and smooth and has nearly scale-invariant temperature and density variations.

Since the release of the Planck data, cosmologists find themselves in a situation much like the following scenario: Imagine you live in an isolated town set in a valley bounded by hills. The only people that you have ever seen in the town are residents, until one day a stranger appears. Everyone wants to know how the stranger got to your town. You consult the town gossip (aka the local oracle), who claims to know that she got here by skiing. Believing the gossip, you consider that there are only two hills that lead to your valley. Anyone reading the guidebook would know the first hill, which can be easily accessed using a ski lift. All pistes there have a steady decrease; the visibility and snow conditions are generally good. The second hill is completely different. It is not included in any standard skiing guidebook. No wonder! Its top is known for avalanches. The one path down to your town is challenging because it begins on a flat ridge that suddenly ends at a steep cliff. Furthermore, there is no ski lift. The only conceivable way of starting to ski down this hill is first to jump from a plane and, using a parachute, land at a particular place on the ridge (with inches of precision) and hit with just the right velocity; the slightest mistake would lead the skier off-track toward a distant valley or trap the skier on top of the hill; in the worst case, an avalanche might begin before the skier reaches the ridge so that the person would not survive. If the town gossip is right that the stranger arrived by skiing, it is only reasonable to conclude that she came down the first hill.

It would be crazy to imagine anyone taking the second path because the chances of successfully reaching the town are infinitesimal compared with the path down the other hill. But then you notice something about the stranger. She has no ticket for the ski lift attached to her jacket. Based on this observation and the town gossip's continued insistence that the stranger arrived on skis, you are forced to the weird conclusion that the stranger must have taken the second mountain. Or perhaps she did not ski in at all, and you need to question the reliability of the town gossip.

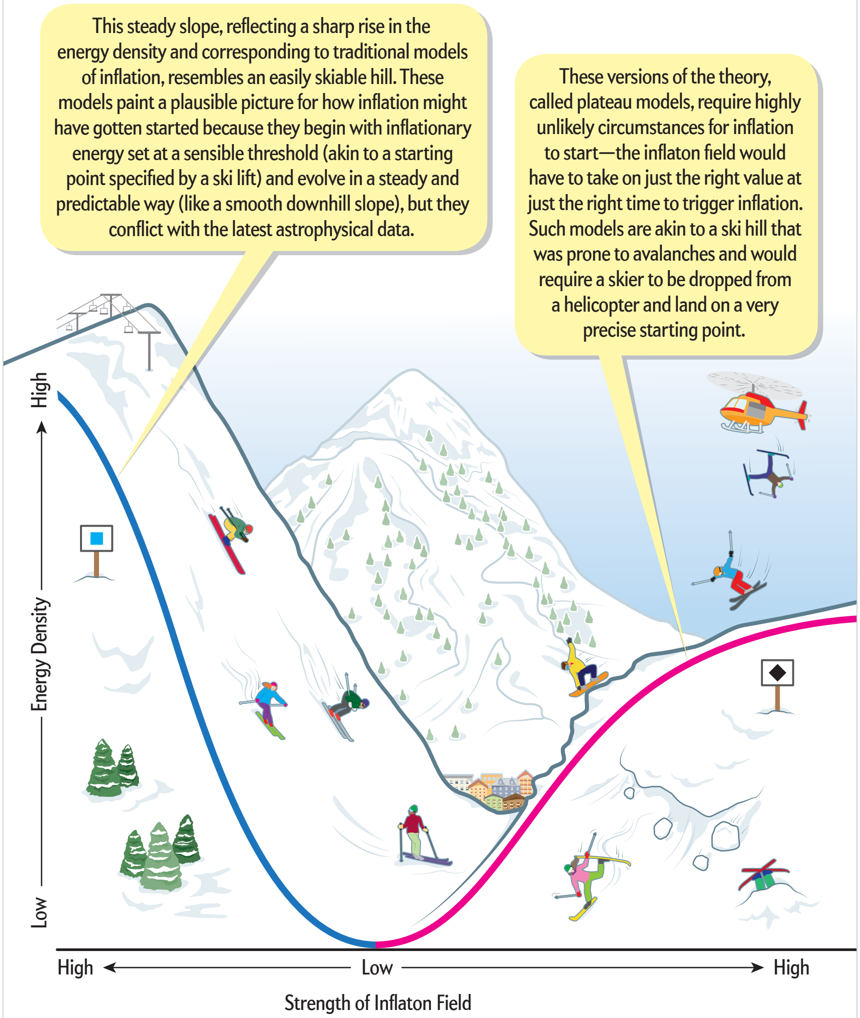
Analogously, if a professed oracle informed us that the universe evolved to its present condition via inflation, we would expect an inflationary energy density curve like the hill described in the guidebooks because it has a simple shape from top to bottom, the fewest adjustable parameters and the least delicate conditions necessary for starting inflation. Indeed, up until now, the textbooks on inflationary cosmology have almost all presented energy curves of this simple, uniform shape. In particular, the energy density along these simple curves steadily increases as the field strength changes so that it is possible to have an initial value of the inflaton field for which the inflationary energy density is equal to a number called the Planck density (10^{120} times greater than the density today), the total energy density available when the universe first emerged from the big bang. With this advantageous starting condition in which the only form of energy is inflationary, accelerated expansion would begin immediately. During inflation, the strength of the inflaton field would naturally evolve so that the energy density slowly and smoothly decreases following the curve down to the valley where the curve bottoms out, corresponding to the universe we inhabit today. (We can think of this progression as the inflaton field "skiing" down the curve.) This is the classic story of inflation presented in textbooks.

But the Planck observations tell us this story cannot be right. The simple inflationary curves produce hot and cold spots with a larger deviation from scale invariance than observed and gravitational waves strong enough to have been detected. If we continue to insist that inflation happened, the Planck results require that the inflaton field "skied" down a more complicated energy density curve shaped like the second hill, the one with high avalanche risk and a low, flat ridge ending with a steep cliff down to a valley. Instead of a simple, ever rising shape, such an energy curve would rise sharply (forming a cliff) away from its minimum until it suddenly flattened out along a plateau (forming a ridge) at an energy density that is a trillion times less than the Planck density available immediately after the big bang. In that case, the inflationary energy density would comprise an infinitesimal fraction of the total energy density after the big bang, far too small to cause the universe to inflate right away.

TWO VERSIONS OF A THEORY

Inflation as a Ski Slope

If inflation took place, it must have been triggered by a hypothetical "inflationary energy," caused by a field called "the inflaton" that would have permeated space. Different versions of inflation theory propose different relations between the strength of the inflaton field and the density of inflationary energy. Two of those relations are plotted here. One (*blue at left*) is akin to the traditional textbook models of inflation; the other (*pink at right*) requires very special starting conditions and thus seems implausible. This analogy with two ski hills offers an idea of why the second class of models—the kind of inflation that has not been ruled out by recent data—is hard to swallow.



Because the universe is not inflating, the inflaton field is free to begin with any initial value and change at breakneck speed, like the skier jumping from the helicopter. Yet inflation can only start if the inflaton field eventually reaches a value corresponding to a point along the plateau and if the inflaton field changes very slowly. Just as it is treacherous for the skier dropped from high altitudes to land on the flat ridge at the right velocity to ski smoothly down, so it is nearly impossible for the inflaton field to reduce its speed at just the right rate and at the right value of the field to begin inflation. To make matters worse, because the universe is not inflating during this period after the big bang when the inflaton speed is slowing, any initial warps or unevenness in the distribution of energy throughout the universe will increase; when they grow large, they prevent inflation from starting no matter how the inflaton evolves, just as an avalanche can block the skier from a smooth downhill ski no matter how perfect the trajectory from the helicopter to the ridge.

In other words, by accepting the oracle's word and insisting that inflation occurred, you would be forced by the Planck data to the weird conclusion that inflation started with a plateaulike energy density curve despite all its problems. Or maybe at this point you would question the oracle's credibility.

THE "MULTIMESS"

THERE IS, OF COURSE, NO ORACLE. We should not just accept the assumption that inflation happened, especially because it does not offer a simple explanation of the observed features of the universe. Cosmologists should evaluate the theory by adopting the standard scientific procedure of estimating the odds that inflation occurred given what we observe about the universe. In this respect, it is undoubtedly bad news that current data rule out the simplest inflationary models and favor more contrived ones. But truth be told, the latest observations are not the first problem encountered by inflation theory; rather these results have sharpened and added a new twist to established issues.

For example, we should consider whether it is reasonable for the universe to have had the initial conditions necessary for *any* kind of inflationary energy whatsoever. Two improbable criteria have to be satisfied for inflation to start. First, shortly after the big bang, there has to be a patch of space where the quantum fluctuations of spacetime have died down and the space is well described by Einstein's classical equations of general relativity; second, the patch of space must be flat enough and have a smooth enough distribution of energy that the inflationary energy can grow to dominate all other forms of energy. Several theoretical estimates of the probability of finding a patch with these characteristics just after the big bang suggest that it is more difficult than finding a snowy mountain equipped with a ski lift and well-maintained ski slopes in the middle of a desert.

More important, if it were easy to find a patch emerging from the big bang that is flat and smooth enough to start inflation, then inflation would not be needed in the first place. Recall that the entire motivation for introducing it was to explain how the visible universe came to have these properties; if starting inflation requires those same properties, with the only difference being that a smaller patch of space is needed, that is hardly progress.

Such issues are just the beginning of our problems, however. Not only does inflation require starting conditions that are difficult to obtain, it also impossible to stop inflation once it gets going. This snag traces back to the quantum fluctuations in spacetime. They cause the strength of the inflaton field to vary from place to place, resulting in some spots in space ending inflation earlier than others. We tend to think of quantum fluctuations as tiny, but as early as 1983, theorists, including Steinhardt, came to realize that large quantum jumps in the inflaton field, though rare, could totally change the inflationary story. Large jumps can increase the strength of the inflaton field to values much higher than average, causing inflation to last much longer. Although large jumps are rare, the regions that undergo them expand enormously in volume compared with regions that do not undergo them and quickly dominate space. Within instants, an area that stops inflating becomes surrounded and

dwarfed by regions still inflating. The process then repeats. In most of the swelled region, the inflaton field strength will change in a way that causes the energy density to decrease and inflation to end, but rare large quantum jumps will keep inflation going in some places and create even more inflating volume. And so the process continues, ad infinitum.

In this way, inflation continues eternally, generating an infinite number of patches where inflation has ended, each creating a universe unto itself. Only in these patches where inflation has stopped is the expansion rate of space slow enough to form galaxies, stars, planets and life. The worrisome implication is that the cosmological properties of each patch differ because of the inherent randomizing effect of quantum fluctuations. In general, most universes will not turn out warp-free or flat; the distribution of matter will not be nearly smooth; and the pattern of hot and cold spots in the CMB light there will not be nearly scale-invariant. The patches span an infinite number of different possible outcomes, with no kind of patch, including

SCIENTIFIC AMERICAN ONLINE Read about advances in bounce theories at ScientificAmerican.com/feb2017/inflation one like our visible universe, being more probable than another. The result is what cosmologists call the multiverse. Because every patch can have any physically conceivable properties, the multiverse does not explain why our universe has the very special conditions that we observe—they are purely accidental features of our particular patch.

And perhaps even this picture is too rosy. Some scientists dispute whether any patches of space evolve into regions like our observable universe. Instead eternal inflation may devolve into a purely quantum world of uncertain and random fluctuations everywhere, even where inflation ends. We would like to suggest "multimess" as a more apt term to describe the unresolved outcome of eternal inflation, whether it consists of an infinite multitude of patches with randomly distributed properties or a quantum mess. From our perspective, it makes no difference which description is correct. Either way, the multimess does not predict the properties of our observable universe to be the likely outcome. A good scientific theory is supposed to explain why what we observe happens instead of something else. The multimess fails this fundamental test.

PARADIGM SHIFT

GIVEN ALL THESE PROBLEMS, the prospect that inflation did not occur deserves serious consideration. If we step back, there seem to be two logical possibilities. Either the universe had a beginning, which we commonly dub the "big bang," or there was no beginning and what has been called the big bang was actually a "big bounce," a transition from some preceding cosmological phase to the present expanding phase. Although most cosmologists assume a bang, there is currently no evidence—zero—to say whether the event that occurred 13.7 billion years ago was a bang or a bounce. Yet a bounce, as opposed to a bang, does not require a subsequent period of inflation to create a universe like the one we find, so bounce theories represent a dramatic shift away from the inflation paradigm.

A bounce can achieve the same end as a bang plus inflation because before the bounce, a span of slow contraction extending for billions of years can smooth and flatten the universe. It may seem counterintuitive that slow contraction has the same effect as rapid expansion, but there is a simple argument that shows it must be so. Recall that without inflation, a slowly expanding universe would become increasingly curved, warped and nonuniform with time from the effects of gravity on space and matter. Imagine watching a film of this process run backward: a large, highly curved, warped and nonuniform universe gradually contracts and becomes flat and uniform. That is, gravity works in reverse as a smoothing agent in a slowly contracting universe.

As in the case of inflation, quantum physics amends the simple smoothing story in bounce theories as well. Quantum fluctuations change the rate of contraction from place to place so that some regions bounce and begin to expand and cool before others. Scientists can construct models in which the rate of contraction gives rise to temperature variations after the bounce that are consistent with the pattern of hot and cold spots observed by the Planck satellite. In other words, contraction before a bounce can do what inflation was supposed to do when it was first invented.

At the same time, bouncing theories have an important advantage compared with inflation: they do not produce a multimess. When the contracting phase begins, the universe is already large and classical (that is, described by Einstein's general theory of relativity), and it bounces before it shrinks to a size where quantum effects become important. As a result, there is never a stage, like the big bang, when the entire universe is dominated by quantum physics, and there is no need to invent a quantum-to-classical transition. And because there is no inflation during the smoothing to cause regions that undergo rare, large quantum fluctuations to blow up in volume, smoothing via contraction does not produce multiple universes. Recent work has produced the first detailed proposals for describing how the universe could have transitioned from contraction to expansion, enabling the construction of complete bouncing cosmologies.

NONEMPIRICAL SCIENCE?

GIVEN THE ISSUES with inflation and the possibilities of bouncing cosmologies, one would expect a lively debate among scientists today focused on how to distinguish between these theories through observations. Still, there is a hitch: inflationary cosmology, as we currently understand it, cannot be evaluated using the scientific method. As we have discussed, the expected outcome of inflation can easily change if we vary the initial conditions, change the shape of the inflationary energy density curve, or simply note that it leads to eternal inflation and a multimess. Individually and collectively, these features make inflation so flexible that no experiment can ever disprove it.

Some scientists accept that inflation is untestable but refuse to abandon it. They have proposed that, instead, science must change by discarding one of its defining properties: empirical testability. This notion has triggered a roller coaster of discussions about the nature of science and its possible redefinition, promoting the idea of some kind of nonempirical science.

A common misconception is that experiments can be used to *falsify* a theory. In practice, a failing theory gets increasingly immunized against experiment by attempts to patch it. The theory becomes more highly tuned and arcane to fit new observations until it reaches a state where its explanatory power diminishes to the point that it is no longer pursued. The explanatory power of a theory is measured by the set of possibilities it excludes. More immunization means less exclusion and less power. A theory like the multimess does not exclude anything and, hence, has zero power. Declaring an empty theory as the unquestioned standard view requires some sort of assurance outside of science. Short of a professed oracle, the only alternative is to invoke authorities. History teaches us that this is the wrong road to take.

Today we are fortunate to have sharp, fundamental questions imposed on us by observations. The fact that our leading ideas have not worked out is a historic opportunity for a theoretical breakthrough. Instead of closing the book on the early universe, we should recognize that cosmology is wide open. SA

MORE TO EXPLORE

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scientificamerican.com/magazine/sa

BIOLOGY

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TAKEOFF: Investigators launch a drone modified to collect airborne microorganisms from a field near Blacksburg, Va.

gh-flying microbes

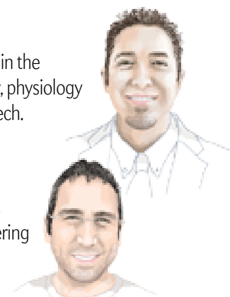
Aerial drones and chaos theory help researchers explore the many ways that microorganisms spread havoc around the world

By David Schmale and Shane Ross

Photographs by Adam Ewing

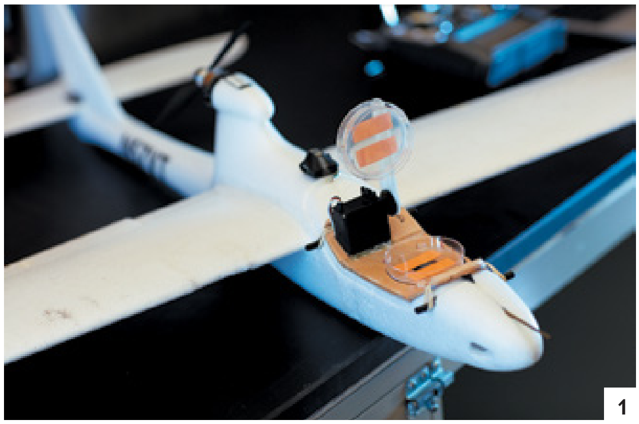
David Schmale is a professor in the department of plant pathology, physiology and weed science at Virginia Tech.

Shane Ross is an associate professor of dynamical systems and fluid dynamics in the department of biomedical engineering and mechanics at Virginia Tech.



The air around us is teeming with microscopic life. With every breath we take, we inhale thousands of bacteria, viruses and fungi.

Scientists have known for almost 150 years that some of these airborne microbes cause disease in plants, domestic animals and people. More recently, we have learned that microorganisms may also affect the weather by allowing water to freeze at warmer temperatures and triggering the onset of precipitation. Astonishingly, a few of these microbes drift on large currents of air to cross oceans and continents. New tools and technology are helping investigators learn more about where these organisms originate, how they spread and the often unexpected ways in which they affect our world during their travels.



1

For more than a decade the two of us have been chasing some of the pathogens that are particularly harmful to agricultural crops, causing billions of dollars in losses around the globe every year from a wide range of ailments, including blight and poisoning by toxins. One of us (Schmale) studies the aerobiology of microorganisms that cause plant disease; the other (Ross) develops mathematical models that describe and predict how currents of air move across short and long distances. We teamed up in 2006 to trace the routes by which plant pathogens spread from one field, region or continent to the next.

To that end (and unique to our collaboration), we deploy a small fleet of airborne drones equipped with sampling devices to collect and analyze the microbes from the lower atmosphere. Every sampling mission turns up a wide range of interesting organisms—many either not well studied or previously unknown to science. We have developed new tools for understanding the long-distance transport of microorganisms in the atmosphere and formed new hypotheses about how far some microbes might travel with the wind and how they might help trigger rain, snow and other forms of precipitation.

Eventually our work may enable agricultural officials to monitor disease-causing microorganisms in the air, predict where they might travel and thus identify which fields to treat or quarantine. Such information will allow farmers to decide, among other things, which crop varieties to plant or when to spray fungicides or other compounds to protect their yields. We have focused much of our research on one pathogen in particular, *Fusarium graminearum,* a fungus that has spread farther and faster over the past few decades than ever before thanks in part to climate change and no-till practices that have increased crop residue in fields, allowing the infection to persist from one year to the next. Whenever agricultural experts, ourselves included, worry that further global warming could significantly threaten the world's food supply in the near future, we are thinking about the explosive spread of this and other fungi that render grains unfit for consumption.

TOXINS IN YOUR FOOD

MANY PEOPLE ARE UNAWARE of just how devastating disease-causing microbes can be to agriculture. One of the worst plant ailments

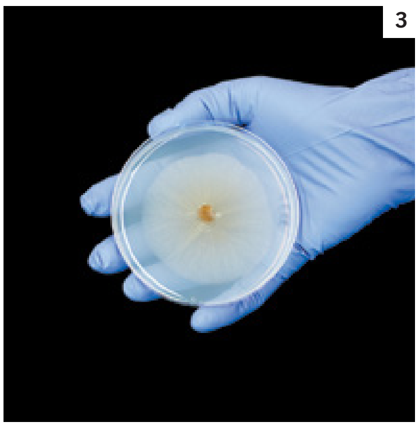
IN BRIEF

One of the most widely devastating crop ailments is fusarium head blight (FHB), which primarily affects barley, oats and other small grains and which has been spreading into new regions of the globe in a changing climate.

Because the fungus that causes FHB travels through the air, the authors deployed drones and developed sophisticated simulations to try to determine how far these pathogens can travel. The latest findings show that these microorganisms can be transported by various weather systems for tens to hundreds of kilometers along intricate and ever changing highways in the sky.

The work may eventually help farmers protect their crops by monitoring the spread of plant pathogens and determining the most effective countermeasures.

2



3

FLIGHT PLAN: Drones used to study microbes in the lower atmosphere carry specially adapted petri dishes that can be opened and closed from the ground (*1*). A drone flies a preprogrammed route (*2*). And a spore collected from the air grows into a pure culture of *Fusarium* in the lab (*3*).

is fusarium head blight (FHB, commonly referred to as scab), which bleaches the heads of wheat, barley, oats, and other small grains and fills the kernels with chemicals called mycotoxins. When ingested in large enough amounts, these mycotoxins make people and livestock very sick, often causing them to vomit. Because grain containing the toxins often cannot be separated from healthy grains, harvested crops must be tested and destroyed if they contain more than a trace amount of toxins.

Several different species of the fungal genus *Fusarium* cause FHB around the world. *Fusarium asiaticum* has long been a problem in central China, from which it has recently begun spreading northward. *F. graminearum* is predominant in the U.S., where it wreaked havoc in corn in the 1970s, causing many pigs to become sick (this outbreak led to the discovery of the mycotoxin deoxynivalenol, which causes pigs to vomit and refuse to eat their feed). Because controlling FHB is so expensive, it has rendered the planting and harvesting of wheat increasingly unprofitable in many states in the U.S. where wheat is commonly grown.

F. graminearum survives winter by hiding out in plants that are left lying on the ground after the previous year's harvest. In the spring and summer, fungal structures called perithecia develop on these residues and forcibly discharge *Fusarium* spores into the air. These spores, in turn, land on the newly emerging anthers of wheat and silks of corn. The spores germinate, and the fungus spreads through the plant, ultimately leading to the accumulation of mycotoxins in the grain. The cross-contamination from one crop to another is why agriculture extension agents advise farmers to avoid planting wheat in fields immediately after they have been used to grow corn or other crops that are susceptible to FHB.

WALLS OF AIR

ONE OF THE GOALS of our collaborative research is to understand how microorganisms are transported over long distances in the atmosphere. As a first step, we decided to measure how far *F. graminearum* can move through the air from an infected field over the course of a day or night.

With funding from the U.S. Wheat and Barley Scab Initiative and the Virginia Small Grains Board, we conducted a series of experiments in commercial wheat fields in Virginia. We took one particular strain of *F. graminearum* that we had isolated from elsewhere in the state and characterized it down to the level of its DNA. In this way, we could distinguish it from the strains that already existed in the fields that we were about to study. Then we spread cornstalks infested with our test fungus over an area about the size of half a hectare and set out a series of petri plates to capture any potential *Fusarium* spores at various distances on the ground from the site of inoculation.

In one set of experiments, we recovered spores from our test strain almost one kilometer from where it had originally been released. But there was no telling how much farther some of the spores might have traveled because one kilometer was the limit of our recovery effort. At any rate, it now seemed clear that *Fusarium* spores could travel much farther than most researchers had previously anticipated.

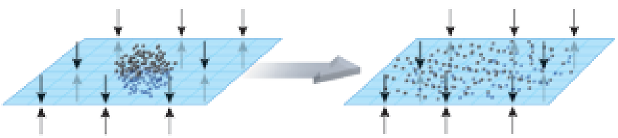
Rather than just continuing to distribute petri plates on the ground farther and farther afield around the state to look for our unique *Fusarium* spores, we decided to search for microorganisms in the air above the fields we studied. The higher up we found the microbes, the more likely we could turn to some of the complex mathematical calculations that meteorologists use to track

BASICS

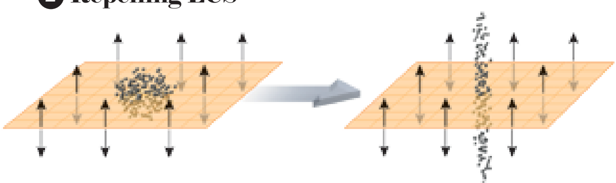
Walls of Air

The movement of air, like that of other fluids, creates certain patterns—such as the Atlantic jet stream—whose shape is influenced by temporary "walls," known as Lagrangian coherent structures, or LCSs, made of air. These features fall into two main categories: walls that mostly attract air currents (and any particles they contain) and walls that mostly repel nearby parcels of air. The complex mathematics that governs these structures (*depicted below in blue and orange*) determines whether a mass of particles—such as fungal spores—eventually scatters all along the wall's surface 1 or forms a column on either side of the LCS 2.

1 **Attracting LCS**

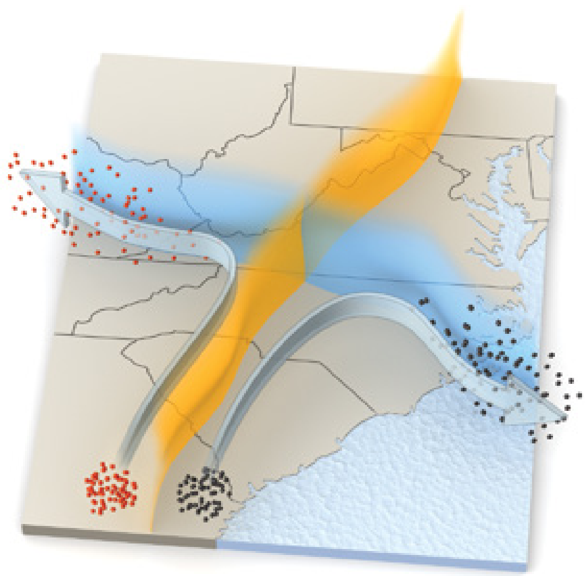


2 **Repelling LCS**



LCS Walls Create Different Patterns of Airflow

The intersection of an attracting LCS (*blue*) with a repelling one (*orange*) creates a particular flow of air known as a saddle point. In the example below, two groups of particles that start fairly close to each other travel hundreds of miles in opposite directions once they hit the center of the saddle point.



weather to determine how far they could theoretically travel.

Thus, we customized a number of drones (unmanned aerial vehicles) with unique sampling devices to collect and analyze microorganisms during flight. With funding from the Emerging Frontiers and Dynamical Systems programs of the National Science Foundation, we used the drones to collect some of the *F. graminearum* spores that were already floating over our heads in Virginia. Analyzing the resulting data suggested that some of these fungi had been airborne for several hours—long enough to have been stirred by large-scale weather patterns spanning hundreds of kilometers.

Further investigation revealed that short-lived, invisible moving "walls of air" play a major role in determining how far these fungi travel and where they land. These atmospheric features, formally known as Lagrangian coherent structures (LCSs), arise whenever different currents of air (or any other fluid, for that matter) run into one another or travel around an obstacle, such as a mountain or the wing of an airplane. The currents' initial direction and speed at the moment of contact determine where various air particles will travel next, creating patterns that can be simulated by computers, using the complex mathematics of chaos theory and a specialized branch of physics known as nonlinear dynamics.

As you might expect, these temporary walls of air drive much of the weather we see on any given day. Intricate, ever changing LCS patterns have been shown to shape, concentrate and divide the air over the Atlantic Ocean, for example, in such a way that the winds of a hurricane either gather strength or dissipate as the storm moves over the water. Less extensive interfaces determine how airborne pathogens climb, dive and swirl through a valley, sometimes landing on one farm but not the adjoining property. By tracking LCSs over time and space, we have formulated hypotheses about where various microbial threats to a particular region are likely to come from and where they might go next. As we get better at developing this information, farmers may find it as useful to consult our microbial forecasts as they do the weather report.

Fusarium fungi are just the tip of the iceberg. Because microbes travel through the atmosphere, they clearly do not respect international boundaries. A deadly strain of wheat stem rust (Ug99) has been bouncing around the African continent from its origins in Uganda since the late 1990s; growers in Australia and North America are particularly worried about its potential arrival via regular atmospheric currents over the Indian and Atlantic oceans, respectively. Soybean rust initially rode into the U.S. from South America on Hurricane Ivan in 2004; it currently hides out in the U.S. South during the winter and makes its annual entry into the Northeast and the Midwest via predictable air routes each growing season (the fungus is unable to survive harsh winters). A coalition of agricultural stakeholders has even established a national monitoring network to keep tabs on this pathogen's seasonal spread every year.

Intriguingly, many of these microbes could not survive such long journeys through the atmosphere on their own. For one thing, prolonged exposure to the ultraviolet radiation of the sun can kill them. But microbes that manage to attach themselves to dust particles can be shielded from the sun's sterilizing glare. Scientists such as Dale Griffin of the U.S. Geological Survey have documented several well-established lanes of global dust trans-

Illustration by Emily Cooper

port, which connect Africa to Europe and Asia, for example, or Asia to the U.S. Indeed, an estimated hundreds of millions of tons of Saharan dust—and their attendant microbes—land in Florida every year. Besides setting off hazy days and stunning sunsets, these dust clouds could unleash serious ecological destruction in their wake. Recent work has suggested that some causal agents of coral disease in the Caribbean—aspergillosis of sea fans in particular—may have been transported in African dust. The increasing desertification of northwestern Africa compounds the danger as more and more marginally arid land turns to dust that can bear and shield a greater number of plant-killing microbes half a planet away.

WIND AND WATER

MICROBES DO NOT JUST SPREAD DISEASE while traveling in the sky. They may also help create the weather over land, lakes and oceans. Meteorologists have long known that hail, snow and rain typically fall from the sky only after the formation of tiny ice crystals in clouds. Whether a snowflake or a raindrop forms around the ice depends on certain environmental conditions, including the presence of particles—such as soot—that allow water to freeze at warmer temperatures than usual. (Pure water freezes at temperatures as low as about –38 degrees Celsius.)

In 1982 David Sands of Montana State University and his colleagues posited that something else—namely the bacterium *Pseudomonas syringae*—could also serve as the nucleus for ice crystals in the atmosphere. Subsequent research hinted at a possible mechanism. Certain strains of *P. syringae* produce a particular protein on the cell's surface that traps water molecules in such a way that they start creating a crystal lattice. On the ground, strains producing these ice-forming proteins can cause frost damage to crops. But the microbes can also soar aloft into clouds where the temperature is far below zero degrees C. If enough of these bacteria produced sufficient ice-nucleating proteins in the sky, Sands thought, they could conceivably trigger the formation of raindrops or snowflakes.

Or at least that is the idea. Since Sands's paper, researchers have found plenty of *P. syringae* in bulk samples of rain and snow. Whether the microbes are primarily responsible for the onset of precipitation or mostly tagging along for the ride is tough to prove. Ski resort operators are not waiting for a definitive answer, however: many of them use commercial ice nucleators that contain bits of *P. syringae* to create artificial snow during warm winter days.

Sands's hypothesis inspired us to see if we could find any other microorganisms in the atmosphere that might initiate precipitation. Supported by the Dimensions of Biodiversity program of the National Science Foundation, research conducted by Schmale and his colleagues has shown that microbes associated with precipitation are far more diverse than originally expected. In Virginia, Boris Vinatzer and Schmale have collected many different types of bacteria and fungi in the atmosphere and in precipitation that can serve as ice nucleators, at least in the lab. And the diversity of microbes associated with precipitation appears to differ depending on geographical location. A better understanding of why each of these microbes predominates in different regions could help us better predict weather patterns. And perhaps we could eventually use some of these microorganisms to develop tools for making it rain in arid regions or areas beset by drought.

MICROBE CATCHERS: Ross (*left*) and Schmale (*right*) study the transport of microorganisms along highways in the sky.

Ultimately we hope to combine what we have learned about microorganisms in water droplets with our calculations about Lagrangian coherent structures to describe what happens in the air immediately above the surface of lakes, rivers and oceans. We have already begun collecting microbes over water using teams of unmanned boats and aerial drones. The mathematical equations needed to describe the mixing of microbe-laden air and water from crashing waves, sweeping winds or even the splashing impact of rain are more complex than anything we have attempted so far. Because water covers about 70 percent of the planet, however, we have no doubt that what we find will reveal fascinating new ways that microbes travel the globe. SA

MORE TO EXPLORE

Mycotoxins in Crops: A Threat to Human and Domestic Animal Health. David G. Schmale III and Gary P. Munkvold in *Plant Health Instructor.* Published online 2009. www.apsnet.org/edcenter/intropp/topics/Mycotoxins/Pages/default.aspx

Life in the Clouds. Lesley Evans Ogden in *BioScience,* Vol. 64, No. 10, pages 861–867; October 2014.

Highways in the Sky: Scales of Atmospheric Transport of Plant Pathogens. David G. Schmale III and Shane D. Ross in *Annual Review of Phytopathology,* Vol. 53, pages 591–611; August 2015.

The Surprising Importance of Stratospheric Life. Chelsea Wald in *Nautilus,* No. 37, Chapter 1; June 2, 2016. http://nautil.us/issue/37/currents/the-surprising-importance-of-stratospheric-life

FROM OUR ARCHIVES

Walls of Water. Dana Mackenzie; July 2013.

scientificamerican.com/magazine/sa

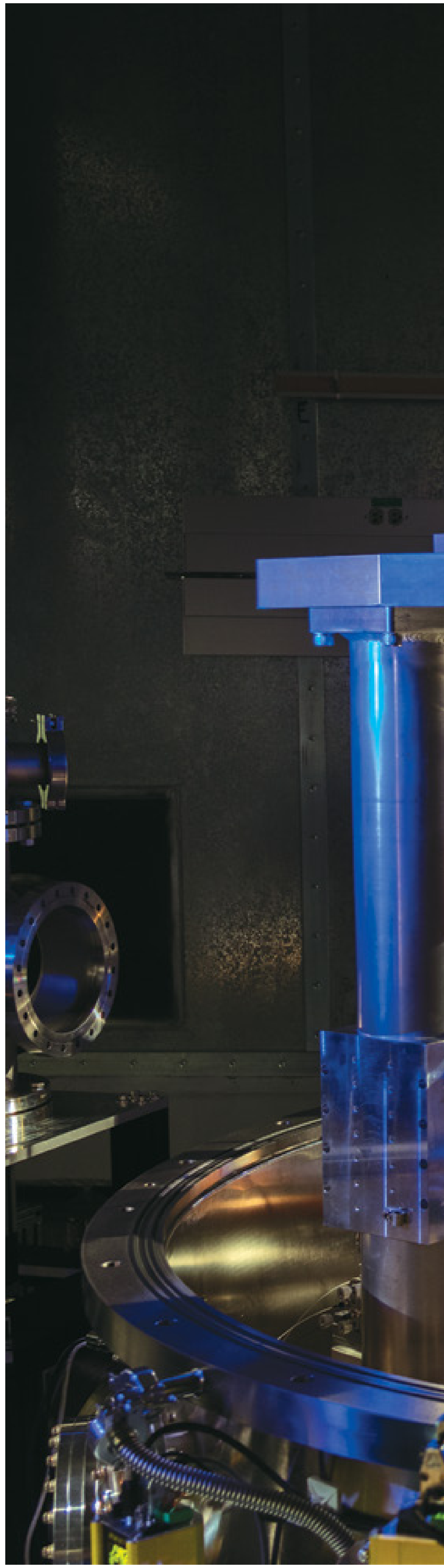
SCIENTIFIC AMERICAN ONLINE Watch Schmale describe different ways that microbes surf the air at ScientificAmerican.com/feb2017/drone

METROLOGY

MASS HYSTERIA

THE LONG-RUNNING EFFORT TO DITCH THE DECAYING, 19TH-CENTURY ARTIFACT THAT DEFINES THE KILOGRAM NEARS ITS CONCLUSION

By Tim Folger



Photographs by Richard Barnes

KIBBLE BALANCES, such as the U.S. National Institute of Standards and Technology's NIST-4, compare electrical and mechanical power. They are finicky and central to the kilogram-redefinition process.

Tim Folger writes for *National Geographic, Discover* and other national publications. He is also the series editor for *The Best American Science and Nature Writing,* an annual anthology published by Houghton Mifflin Harcourt.

AS HE APPROACHED THE SECURITY CHECKPOINT AT Washington Dulles International Airport one afternoon last April, Jon Pratt felt on edge. Stuffed in his camera bag were four solid-metal cylinders, the sorts of objects guaranteed to draw the scrutiny of wary Homeland Security TSA staff. Each cylinder weighed exactly one kilogram. One of them—a gleaming platinum-iridium alloy about half the size of a can of tuna—was worth at least $40,000. (The price of platinum currently hovers around $1,000 per troy ounce, a common unit for precious metals.) The other three consisted of finely machined stainless steel.

PRATT'S MISSION: Deliver them safely—and untouched—to a colleague in a Parisian suburb.

Pratt held documents from the National Institute of Standards and Technology meant to ease his way through security. The paperwork explained that he carried four official U.S. kilograms—the reference masses that serve as the basis for all weight measurements in the country—and specified that the kilograms should not be touched or removed from their protective canisters.

A slender former punk rocker, Pratt runs NIST's Quantum Measurement Division in Gaithersburg, Md. "The TSA guy was giving me a bit of a hard time," he says. "But then he read all the literature, and it became this cool thing that made his day." After a few minutes, Pratt was waved through and boarded the flight for the seven-hour trip to Paris, which presented another dilemma: What to do with his costly carry-on if he needed to get up? Should he keep the bag with him at all times, as some colleagues had advised? "I will admit that I left it parked beneath the seat in front of me while I went to the bathroom," Pratt says. "So it was out of my sight briefly, and someone may have come over and rubbed their hands all over the kilograms."

Such handling would have spoiled many months of careful work devoted to measuring the kilograms to an accuracy of a few parts per billion. Pratt was taking the cylinders to the International Bureau of Weights and Measures (BIPM) in Sèvres, a city just across the Seine from Paris. A few months later metrologists there would compare them with identical metal cylinders from three other countries, along with a one-kilogram sphere of highly purified silicon manufactured at Germany's national metrology laboratory. It was the latest step in a historic shift in the way the world measures mass.

Since 1889, the same year the Eiffel Tower opened, the kilogram has been defined by the mass of a platinum-iridium cylinder kept underneath three nested glass bell jars in a vault at the BIPM's headquarters. The International Prototype Kilogram, aka IPK or *Le Grand K,* is the ur-kilogram from which all other national mass standards are derived. The kilogram is an anomaly; it is the last unit of measurement still tied to a physical object—but not for much longer. By the end of 2018 *Le Grand K* will be deposed, and the kilogram will have a new definition based on Planck's constant, a fixed quantity from quantum theory related to the amount of energy carried by a single particle of light, or photon.

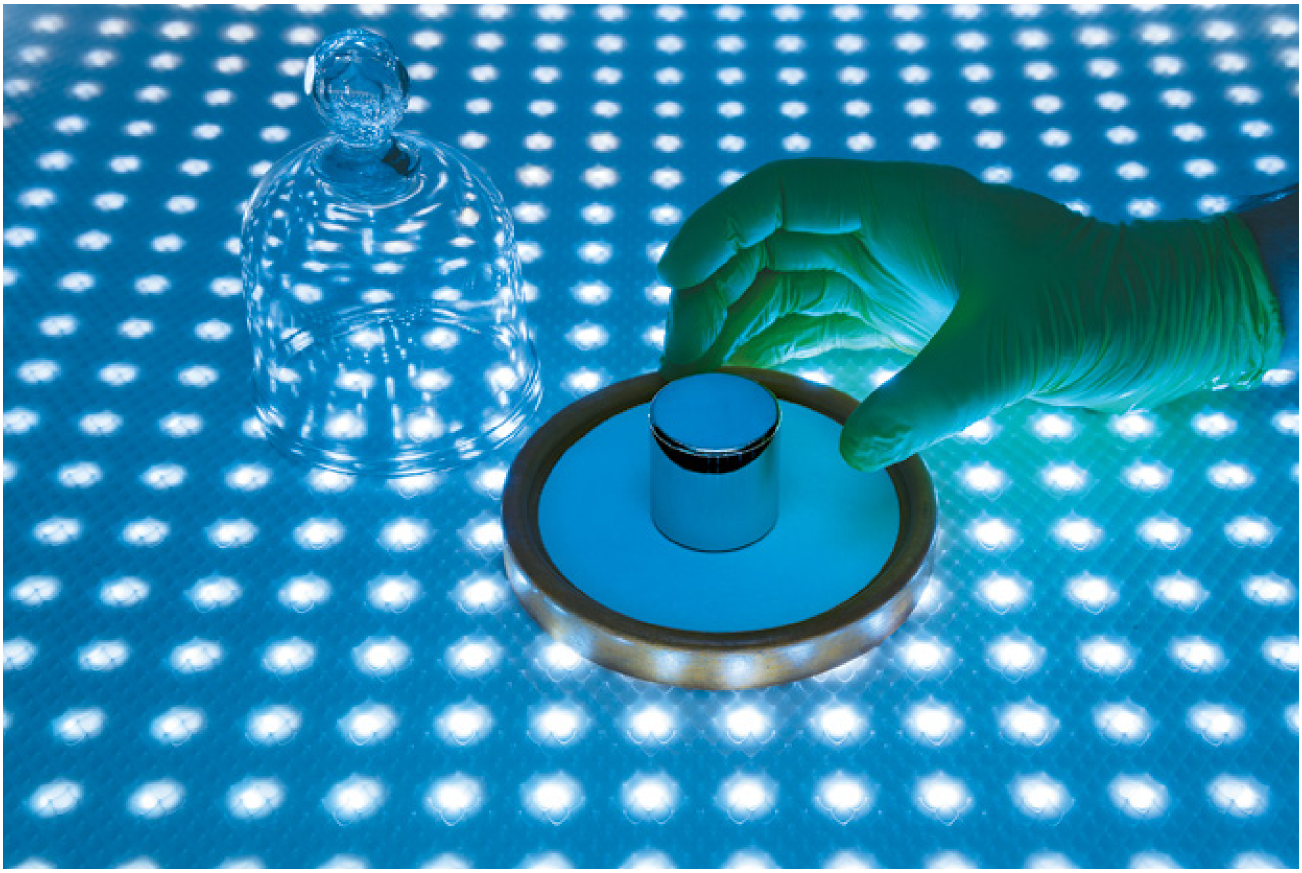
Why force *Le Grand K* into retirement? For years metrologists have wanted the accuracy and reliability of an international mass standard linked to a fundamental constant of the universe rather than a Victorian-era lump of cosseted metal. But there is a more pressing reason for the change: *Le Grand K* appears to be losing mass. Once every 30 years or so *Le Grand*

IN BRIEF

Since 1889 the kilogram has been defined by reference to a single platinum-iridium cylinder held in a secret vault in Paris. It is the last unit of measurement still tied to a physical artifact.

But the ur-kilogram is losing mass. That, in part, is why the General Conference on Weights and Measures decided in 2011 to redefine the kilogram by pegging it to a quantum-mechanical constant.

This year the process of redefinition, which involves the official metrology laboratories of five nations and some of the most difficult measurements in all of science, enters its final phase.



K20, the U.S. national kilogram, is now calibrated against the International Prototype Kilogram in Paris. After redefinition, metrologists will instead use the NIST-4.

K is removed from its vault for cleaning and for comparison with six official copies, or *temoins* ("witnesses"), which are kept in the same vault. When the first two *temoins* were compared with *Le Grand K* in 1889, both matched the original. But measurements made shortly after the World War II and again in 1992 found that the copies outweighed *Le Grand K* slightly. It seems implausible that the copies would all somehow gain mass while *Le Grand K* remained unchanged. There is, of course, a more likely explanation. "We could assume," says BIPM director Michael Stock, "that the International Prototype Kilogram is losing some mass." That uncertainty is one of the reasons the General Conference on Weights and Measures—the governing body of the bureau—decided in 2011 to establish a new mass standard.

No one knows why *Le Grand K* might be shedding weight. It is far too valuable to undergo tests that might provide answers. The mystery presents real problems. As technology advances in the decades ahead, precision measurements of mass on the molecular scale and below will become routine in a wide range of industries. "We will want to have ways to measure microgram masses with at least three-digit resolution," Pratt says. "And with an artifact kilogram, things get really uncertain at small scales."

Le Grand K's shortcomings are not limited to measurements of mass. Units of force and energy are ultimately derived from it as well. "We are now at the point where we would see values of fundamental *constants* change because the IPK changes," Stock says. "And that makes no sense."

THE NEW STANDARD

THE KILOGRAM is the latest of the metric system's seven basic units to be revamped, but it will not be the last. Besides the kilogram, the International System of Units, or SI, comprises the meter, the ampere (for electric current), the second, the candela (a measure of the intrinsic brightness of a light source), the mole (which relates the weight of a substance to the number of atoms it contains), and the kelvin (for temperature).

Two of the SI units were redefined decades ago. In 1983 the meter, formerly gauged by the distance between two lines etched in a solid platinum-iridium bar stored in the same vault as *Le Grand K,* became instead the distance traveled by light in 1/299,792,458th of a second. And with the advent of improved atomic clocks in the 1960s, the second—which had been defined as a fraction of a day—was reset in terms of a specific frequency of microwave radiation emitted from a cesium atom. The mole, kelvin and ampere are all slated for an overhaul in 2018 as well.

The current (so to speak) state of the ampere is especially odd. Its official definition, part of which involves two infinitely long, one-dimensional, massless wires, is so abstract that it

Changing Measures

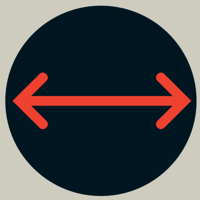
The International System of Units (SI), otherwise known as the metric system, rests on a foundation of seven base units. (Another 22 units are built from those seven.) In 2018 the International Committee for Weights and Measures is expected to redefine the majority of the base units in the biggest overhaul of the metric system since 1960. The move would tie the seven base units to invariant natural constants. The meter, the second and the candela will remain essentially the same, but the other four will be fundamentally reconceived.

Currently Defined in Terms of Physical Constants

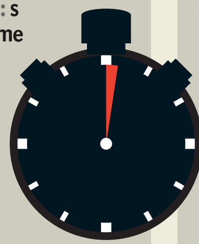
Unit: **Meter**
Abbreviation: **m**
Measures: **Length**

Current definition (established in 1983):
The distance light travels in a vacuum in 1/299,792,458 of a second.

Historical note:
When the French Academy of Sciences proposed the metric system in 1791, it defined the meter as one ten-millionth of one fourth of Earth's circumference, which in turn was defined as a meridian that runs from the North Pole to the equator through—where else—Paris.



Unit: **Second**
Abbreviation: **s**
Measures: **Time**



Current definition (established in 1967):
The second is "the duration of 9,192,631,770 periods of the radiation corresponding to the transition between the two hyperfine levels of the ground state of the cesium 133 atom."

Historical note:
The original definition is the familiar one: a second was 1/86,400 of the "mean solar day," or the time it takes Earth to rotate relative to the sun. The committee gave the second its current, quantum-mechanical definition in 1967.

Unit: **Candela**
Abbreviation: **cd**
Measures: **Luminosity**

Current definition (established in 1979):
A candela is the "luminous intensity, in a given direction, of a source that emits monochromatic radiation of frequency 540 × 10^{12} hertz and that has a radiant intensity in that direction of 1/683 watt per steradian," which is the SI unit for a solid angle.

Historical note:
In the early 20th century the U.S., France and the U.K. defined the candela by referring to the luminosity of a carbon-filament lamp. In 1933 metrologists made the definition more precise by basing it on blackbody radiation. Such a definition was adopted in 1948 and later replaced with the current one.

cannot be replicated in a lab. That will change in 2018 when the ampere is redefined in terms of the charge of an electron, an advance made possible by the development of nanotechnology devices capable of counting individual charged particles moving through a circuit.

"If we look to the next redefinitions, they might include a quantum mechanically based candela for light and maybe an optical definition of the second instead of a microwave definition," says Alan Steele, Canada's chief metrologist. "But those are at least 15 years away. Maybe longer."

The redefinition of the kilogram is the centerpiece of an effort to create a truly universal system of measurement that is not bound to parochial, earthly conventions. In principle, the new units would make sense to intelligent beings anywhere, from here to Andromeda. For metrologists, these are heady times. "This is a once-in-a-lifetime thing," Steele says. "The last time we attempted anything this fundamental was when the meter was redefined. This is the time to be a chief metrologist, I'll tell you that. It's not like world peace or anything, but it's pretty cool."

THE VAULT

LE GRAND K was not the first official kilogram. It has a predecessor, made during the French Revolution, when the entire metric system was born. Before the revolution, local custom determined nearly all of France's weights and lengths. Standards varied from one town to the next, burdening the country with more than 700 different units of measurement. A *toise,* for example, was the equivalent of an English fathom: the distance between a man's outstretched arms. But a Parisian *toise* (which equaled 72 *pouces*) might not have matched one used in Marseilles. *Savants,* as the French then called their scientists, sought to end the chaos by creating a new system "for all people, for all time," a motto memorialized on a contemporary plaque.

"Their idea in 1791 was that the standards should be based on natural and invariable phenomena," says Richard Davis, a retired director of the BIPM's mass division, which is responsible for maintaining *Le Grand K.* "We're still doing that," he says. The difference is that now metrologists are turning to natural constants that really are invariant.

We are sitting in Stock's office in the Pavillon de Breteuil, an elegant 17th-century building on a verdant hilltop overlooking the Seine in Parc de Saint-Cloud, once a royal hunting reserve for French kings. Marie Antoinette's rose garden is still carefully tended here. It has been the headquarters of the international bureau since the Meter Convention of 1875, a treaty signed by 17 nations.

"Did you notice the island on the left as you walked across the bridge to Sèvres this morning?" Davis asks. The island, he says, once housed a Renault factory that built tanks for the German army in World War II. American bombers repeatedly targeted it. After one bombing run rattled the Pavillon de

Illustration by Nigel Holmes

Still to Be Redefined

Unit: Kilogram
Abbreviation: kg
Measures: Mass

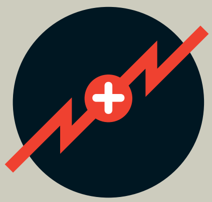
Current definition (established in 1889):
For now the kilogram is still defined by reference to *Le Grand K,* the platinum-iridium cylinder hidden in a vault in Paris.

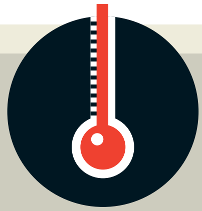
Proposed redefinition:
If efforts remain on schedule, in 2018 the kilogram will be pegged to Planck's constant, a fixed quantity from quantum theory that specifies the amount of energy carried by a single particle of light, or photon.

Unit: Ampere
Abbreviation: A
Measures: Electric current

Current definition (established in 1946):
The ampere's current definition, which involves, among other things, "two straight parallel conductors of infinite length, of negligible circular cross section … placed 1 meter apart in vacuum," is impossible to replicate exactly in the lab.

Proposed redefinition:
The ampere would be simplified by fixing the numerical value for the charge carried by one proton (the fundamental constant known as the elementary charge).





Unit: Kelvin
Abbreviation: K
Measures: Temperature

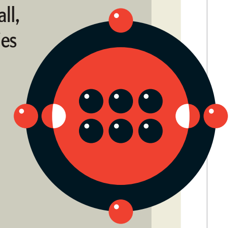
Current definition (established in 1967):
Today one kelvin is equivalent to "1/273.16 of the thermodynamic temperature of the triple point of water"—the combination of temperature and pressure at which ice, water vapor and liquid water can coexist.

Proposed redefinition:
Basing the kelvin on a fixed value for the Boltzmann constant, which relates the average kinetic energy of a gas's molecules with its absolute temperature, would improve the accuracy of extremely low- and high-temperature measurements.

Unit: Mole
Abbreviation: mol
Measures: Amount of substance

Current definition (established in 1971):
"The mole is the amount of substance of a system which contains as many elementary entities as there are atoms in 0.012 kilogram of carbon 12."

Proposed redefinition:
The mole's link to the kilogram would be severed, and the unit would be defined by fixing the numerical value for the Avogadro constant, which refers to the number of molecules, atoms or any other small, discrete quantities of matter in one mole of substance.



Breteuil, *Le Grand K* was placed in a special shockproof container. Although the *temoins* had been evacuated to an underground safe in the Bank of France for most of the war, the Meter Convention specified that *Le Grand K* must always remain at the bureau.

When *Le Grand K* was removed from its vault after the war, in 1946, for cleaning and comparison with the six copies, it was found to be 30 micrograms lighter than the *temoins.* By the time of the next cleaning, 45 years later, the difference had increased to 50 micrograms—the weight of a fly's wing.

"Fifty micrograms—over a century," Stock says, as we look at a graph of the changes on his office computer. "You can see it's very small." For now, he says, the discrepancy does not present any practical difficulties. "But if we continued like this, one day this would lead to problems."

In the realm of nanotechnology, 50 micrograms is a huge number. Moreover, the uncertainty in the kilogram's mass would ripple through a long chain of fundamental units: the metric unit of force—the newton—is defined in terms of the kilogram, and the newton, in turn, defines the joule—a unit of energy—and the joule defines the watt, and so on. Ultimately a small question mark would taint nearly every measurement of the physical world.

Cleaning and comparing *Le Grand K* with the test masses is not a routine task—especially because it has been done only four times since 1889. First *Le Grand K* must be removed from its *caveau,* or vault, which requires the presence of three people to open three locks that are arranged vertically. Inside the vault sits a large safe with a combination lock that holds the *Le Grand K,* which rests under the three nested bell jars. The safe also shelters the six copies. Only three people in the world hold keys to the vault: the BIPM director, the director of the National Archives in Paris and the president of the International Committee for Weights and Measures (CIPM), which supervises the bureau's work. Because each key is different, all three officials must be present to unlock the vault.

"I'm only the second person outside of Europe in the history of the Meter Convention of 1875 that's been elected president of the CIPM," says Barry Inglis, an Australian electrical engineer. "I asked them what happens if I'm traveling home over the Indian Ocean and the plane goes down: 'How are you guys going to manage?' But I'm sure there's a locksmith that could pick the old lock without too much trouble."

Few of the bureau's staff have ever glimpsed *Le Grand K,* and there are rumors that its official photographs depict a stunt double. "I've seen it once," says Susanne Picard, who has worked at the BIPM since 1987. The three key holders open the vault once a year to look at—but not touch—*Le Grand K* to make sure it is, well, still there.

After entering the inner sanctum of *Le Grand K,* a technician picks up the shiny cylinder with chamois-padded tongs and carries it to a cleaning station, where it is rubbed with a chamois cloth soaked with alcohol and ether, followed by a rinse from a jet of doubly distilled water. A final puff of nitrogen gas removes any remaining water droplets. The entire process takes about an hour. The bureau has experimented with different cleaning techniques on test masses—using ultraviolet radiation, for example—but those methods actually made the alloy *too* clean. "They seem to remove more dirt than our technique," Stock says. "But afterward the mass is unstable because it is so clean that the surface becomes highly reactive." And that would only make *Le Grand K* less reliable as a standard, so the bureau remains committed to its chamois-rub-and-water-rinse method.

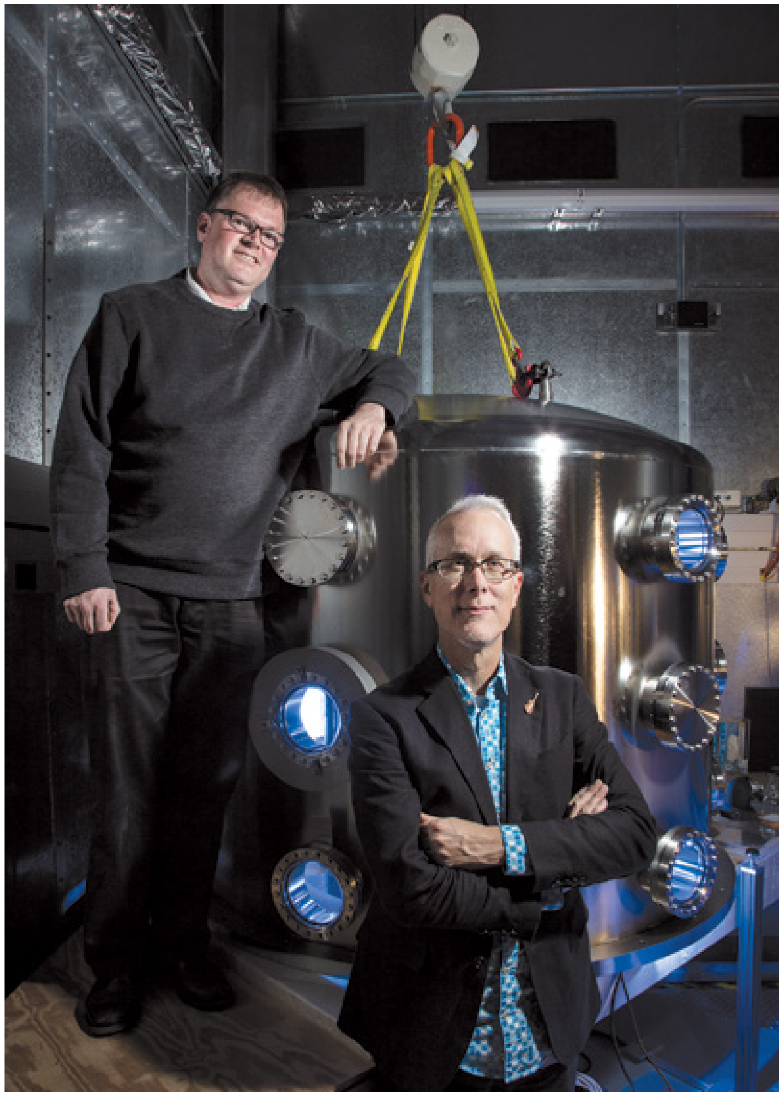
After their baths, *Le Grand K* and the *temoins* are taken to a clean room and put on a device called a mass comparator, a $500,000 instrument that can measure differences in mass as small as one microgram. The mass comparator and 10 so-called working standard kilograms are the workhorses of the BIPM's mass division; they are used for most day-to-day calibrations, with *Le Grand K* and the *temoins* trotted out only once every few decades for verifying national prototype kilograms from different countries.

As the conversation with Davis and Stock winds down, I ask them if I can see the outside of the vault where *Le Grand K* resides; I know there is no chance of seeing the regal master cylinder itself. They burst into laughter, shaking their heads: "No, no, no, no!"

"It's not the first time we've been asked," Davis says.

"It is here on the grounds, right?" I ask.

"Yes," Davis answers, "that much is public knowledge."



METROLOGISTS Stephan Schlamminger and Jon Pratt pose with the NIST-4 Kibble balance, seen here with its 450-kilogram vacuum dome in place.

A TOUGH MEASUREMENT

SOON *LE GRAND K* will be a historical curiosity, and the new international definition of mass will be based on Planck's constant. Planck's constant includes units of both energy and time and can be expressed in terms of mass by massaging the equation $E = mc^2$. Like G, the gravitational constant, Planck's constant arises from theory, but its numerical value can be determined only by experiment. And with better instruments, our measurements of natural constants are steadily improving.

To make the transition to the new quantum standard, the BIPM devised a two-part strategy. First, the national metrology labs of five different countries will fix a numerical value for Planck's constant, weigh their national kilograms in terms of that value and then see how well their kilogram measurements match. This is the test that the bureau ran last summer. Assuming the results, expected early this year, are satisfactory, the study participants will reverse the process and use their national kilograms at their home facilities to fine-tune their measurement of Planck's constant. The exacting new value for Planck's constant will then be used to permanently redefine the kilogram.

Most of this work will involve the use of an exceedingly complex device called a Kibble balance. Until last year, Kibble balances were known as watt balances. Metrologists decided to rename them after the death of their inventor, British physicist Bryan Kibble, in 2016. Kibble-balance experiments are so difficult that in 2012 the journal *Nature* listed them among the five toughest undertakings in physics, right up there with detecting the Higgs boson or gravitational waves.

One day last May, Stephan Schlamminger of NIST drove me to the white two-story building on the edge of the institute's woodsy 235-hectare campus that houses the older of its two Kibble balances, now essentially mothballed since the comple-

SCIENTIFIC AMERICAN ONLINE For more on metrology, visit ScientificAmerican.com/feb2017/kilo

tion of a newer model in 2014. "It's like the *Little House on the Prairie,*" Schlamminger jokes as we pull up in front of the isolated structure. It is here that most of NIST's measurements of Planck's constant occurred, and the new model will work in much the same way.

Any resemblance to a farmhouse vanishes when we step inside. The interior looks like a setting for a steampunk novel, with walls sheathed in copper all the way to the second-floor ceiling. "See all the brass hardware?" Schlamminger says. "No iron." The copper and brass shield the instrument from external magnetic fields. But the magnetic fields generated *inside* the building are powerful enough to erase credit cards. In the middle of a room on the first floor stands a tall support column with a superconducting magnet at its base. When operating, the magnet is cooled with liquid helium.

The actual balance mechanism is on the second floor. It consists of a half-meter-wide aluminum wheel mounted vertically with balance pans suspended by wires from either side. During measurements, one balance pan holds a kilogram mass; a coil of wire is suspended directly below that same pan by three four-meter-long rods. The pan on the other side of the balance holds a counterweight and an electric motor. Two distinct operating modes of the balance are needed to acquire all the values used in the equations that link mass to Planck's constant. In "weighing mode," the downward gravitational force on the test mass is exactly offset by a magnetic field generated by running a current through the coil suspended below the pan. In "velocity mode," the test mass is removed from the pan, and the coil is lifted by the motor in the opposite pan at a steady velocity through a magnetic field created by the balance's superconducting magnets, which induces a voltage in the moving coil.

Kibble-balance experiments are so difficult that the journal *Nature* listed them among the five toughest undertakings in physics, right up there with detecting the Higgs boson or gravitational waves.

The current measured in the weighing mode and the induced voltage from the velocity mode are then plugged into equations from quantum theory that relate current, voltage and electrical resistance to Planck's constant. In short, starting with a known mass of one kilogram, the Kibble balance can determine Planck's constant. Then, with an accurate value for Planck's constant in hand, the balance can be used to measure mass without the need for any kind of physical artifact.

For accurate results, Schlamminger and his colleagues need to account for local fluctuations in air pressure and gravity. The precession of Earth's axis must be included, too, along with tides. "If you don't correct for tides," Schlamminger says, "it's about a 100-parts-per-billion error." Despite its complexity, he observes, the device reminds him of something from another era. When his team was measuring Planck's constant, valves had to be opened and closed in careful order; the pressure inside tanks full of liquid helium had to be checked constantly. "You felt as if you were driving a steam engine," Schlamminger adds, "yet you were doing experiments measuring quantum-mechanical quantities!"

AU REVOIR, LE GRAND K

WHAT HAPPENS NEXT depends on the results from last year's test. Kilogram measurements by three of the five participating national metrology labs must match within 50 micrograms—the current fly-wing uncertainty in the mass of *Le Grand K.* After the pilot study results are published, work on the redefinition will begin in earnest.

If all goes well, the kilogram will then be defined in terms of Planck's constant. The BIPM has set stringent standards for the redefinition: not only must all the measurements of Planck's constant agree to within 50 parts per billion, but at least one must have an uncertainty below 20 parts per billion—a level the Canadians have already surpassed. For the redefinition to take effect in 2018, all the new measurements of Planck's constant must be accepted for publication by July 1, 2017.

And what of *Le Grand K?* It will remain in its vault. Given the complexity of Kibble balances, though, we probably have not seen the last of kilogram artifacts. Rather than regularly making arduous Kibble-balance measurements, the world's metrology labs will, in the decades ahead, use a new generation of prototypes for day-to-day work. The new prototypes are already taking shape at the bureau. But they will be calibrated by Kibble balances, not *Le Grand K.*

So is this the end of the story? Do we now have a kilogram for all people, for all time? Stock is reserving judgment.

"One of my predecessors, a Nobel laureate named Charles Edouard Guillaume, thought the present kilogram would work for 10,000 years," he says. "This was of course overly optimistic. I'm not sure this will be the last redefinition, but it should be good for some time. Maybe not for the next 10,000 years." SA

MORE TO EXPLORE

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NEUROSCIENCE

NEW STUDIES SHOW COSMIC RADIATION COULD BE EVEN MORE DAMAGING TO ASTRONAUTS' BRAINS THAN WE THOUGHT.

CAN HUMANITY STILL LIVE AND TRAVEL AMONG THE STARS?

By Charles L. Limoli

DEEP-SPACE DEAL BREAKER

Illustration by Chris Malbon

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Charles L. Limoli is a neuroscientist and radiation biologist at the University of California, Irvine, School of Medicine. He studies cognitive impairments resulting from a variety of cancer treatments as well as space radiation.

FOR MILLENNIA HUMANS HAVE GAZED INTO THE NIGHT SKY AND DREAMED OF TRAVELING to the stars. Now that people have walked on the moon and lived in orbit on the space station, it seems inevitable that we will venture farther, to Mars, the rest of the solar system and beyond. The dream is common to many cultures and occupies the space agencies of nations around the world.

Yet we know that space is dangerous. Every time astronauts leave Earth, they face extreme cold, the lack of an atmosphere, microgravity and radiation exposure. These hazards have seemed mostly surmountable so far—mere engineering problems to be figured out and risks that brave space travelers willingly take on. Yet new research, by myself and others, has shown that the radiation in space may be more damaging than we thought, particularly to the fragile yet vital human brain. Although scientists have known about the radioactive nature of space for decades, only recently has evidence emerged of how serious the effects of radiation are on the brain and how long they last.

By irradiating mice, my colleagues and I have measured significant and enduring cognitive impairment that is likely to translate to humans as well, potentially endangering the success of space missions. Although astronauts on the relatively low-flying International Space Station are largely shielded from the worst effects by their perch within the edges of Earth's atmosphere, they run the risk of some cognitive damage. The dangers for voyagers to Mars and beyond, however, could be grave.

We currently have a limited ability to mitigate these perils. Improved shielding for spacecraft could block some radiation, but no known material is lightweight enough to be practical. Drugs that could fight the effects of radiation inside the body are only in the early stages. Unless we find a successful solution, humanity's dreams of journeying throughout the solar system and beyond may be forever out of reach.

POWERFUL PARTICLES

COSMIC RADIATION is pernicious—we cannot see or feel it, yet it fills every inch of what looks like empty space and can do significant damage to human tissue. Most dangerous to astronauts are galactic cosmic rays (GCRs), charged atomic nuclei flying at nearly the speed of light that astronomers think originated in the supernova remnants of dead stars. In addition to GCRs, which pervade the cosmos as a uniform field, our sun also ejects protons (ionized hydrogen) of multiple energies. Although protons constitute most of the radiation in space, because of their lighter mass they cause considerably less damage to our bodies compared with heavier particles. Most important, all these particles possess sufficient energy to traverse the hulls of spacecraft and the bodies of astronauts. Whereas the magnetic fields surrounding planet Earth protect terrestrial inhabitants by deflecting most of these cosmic particles away from the surface, travel beyond the magnetosphere leads to unavoidable exposure and the unfortunate consequences of these particles' interactions with human tissue.

The problem with cosmic radiation is that when these particles pass through the human body, they leave behind some of their own energy that "ionizes" atoms in the tissue—that is, knocks electrons off the atoms, causing them to turn from neutral atoms into charged ions. The charged particles then move along their own trajectories, knocking more electrons loose and generating secondary tracks, causing a widening trail of damage.

IN BRIEF

Space travel has always been dangerous, but new research shows that cosmic radiation is even more harmful to the brain than we knew.

Scientists irradiated mice with charged particles simulating the radiation astronauts get in space and found both behavioral declines and neural damage.

Better shielding for spacecraft and space suits or drugs that protect the brain will be necessary to allow humanity a future among the stars.

The heavier the radiation particle, the more energy it will have and the more atoms it will ionize.

The redistribution of these electrons causes some atoms to break their molecular bonds, damaging proteins, lipids, nucleic acids and other vital molecules in the cells and tissues of the body. This removal of electrons forms free radicals—atoms or molecules that lack the full complement of electrons to fill their atomic orbitals, making them highly reactive and eager to pair with other electrons from adjacent atoms or molecules to fill up their orbitals. The free radicals can then react with other molecules in the body, turning them into new chemicals that do not serve their original purpose. When radicals encounter DNA, for example, they can break apart its sugar phosphate backbone or damage the nucleic acid bases.

Scientists measure radiation exposure in "absorbed doses"—the energy lost by the radiation and deposited in the body (per unit of body mass). The SI unit for absorbed dose is the gray (Gy), where 1 Gy is one joule per kilogram. Radiation also comes in different "qualities," which refers to the density of ionization it produces per unit dose. Scientists characterize radiation types by their linear energy transfer (LET), or the amount of energy lost per distance traveled. For example, a dose of high LET radiation is more dangerous than the same dose of low LET radiation because it leaves behind more energy and thus causes more atoms to ionize. The resultant damage is therefore more difficult for the cell to repair and recover from. Because many of the radiation types encountered in GCRs have a relatively high LET, this characteristic has important implications for deep-space travel, which we will discuss later.

Energetic heavier radiation particles can leave tracks of higher radical density and increased destruction from ionizations compared with particles of lower mass. At the molecular level, we find nanometer-wide regions of high radical density that can lead to relatively small volumes containing a large number of damaged sites on critical molecules. Thus, heavier charged particles produce much higher yields of these regions of "clustered" damage compared with photon radiation (such as x-rays and gamma rays). It is this density of damage that makes space radiation more dangerous than traditional types of ionizing radiation found on Earth.

RE-CREATING SPACE ON EARTH

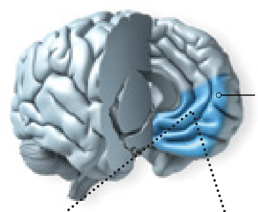
DESPITE THE UBIQUITY of charged particles in space, reproducing these types of radiation fields on Earth to study their effects presents considerable challenges. One of the only places in which we can run experiments simulating space radiation is the NASA Space Radiation Laboratory, a facility NASA and Brookhaven National Laboratory commissioned in 2003 on Long Island. There large particle accelerators speed up ions of various masses to velocities approaching those of space radiation. Experimenters, including myself, place targets—in our case, mice—in the path of this radiation and measure its effects. These tests can show us how specific types of cosmic radiation, at various doses, affect living tissue.

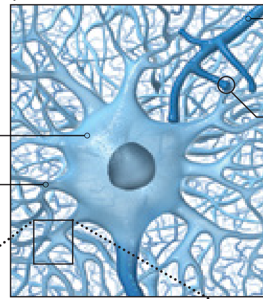
Recently we exposed six-month-old mice to low doses (0.05 to 0.30 Gy) of charged particles (oxygen and titanium, for instance) and tested their behavior. The mice completed tasks called novel object recognition (NOR) and object in place (OiP) to evaluate how the radiation affected their memory and thinking. First, the rodents explored an empty box around three feet square. Then we introduced Legos, rubber ducks and other toys to the box and let the mice wander around a bit more. Later—in some trials after just minutes and in others after hours or a day—we switched the objects for new toys (NOR) or changed the location of the toys (OiP). A smart, healthy animal will seek out novelty and spend

RESEARCH FINDINGS

Space Brain

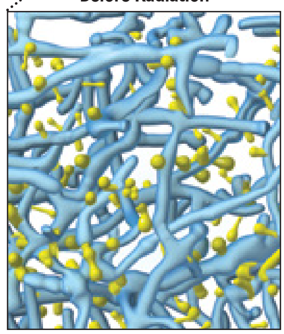
Cosmic radiation may harm astronauts' brains more than previously thought. Scientists exposed mice to an onslaught of charged particles mimicking those that fly through space and measured both behavioral performance and physical damage. The damage was revealed by brain imaging.



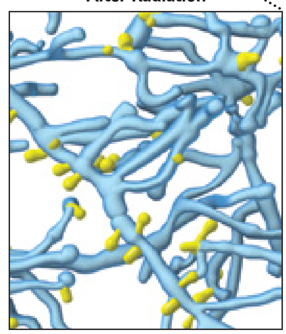


Spacelike radiation damaged a region of the mouse brain called the medial prefrontal cortex, which is associated with memory. In this area, neuron protrusions called dendritic spines decreased in size and number.

Before Radiation



After Radiation



Dendrites receive chemical signals from other neurons. Eight weeks after exposure to 30 centigrays of radiation, the mice showed a 20 to 40 percent reduction in the number of dendritic spines (*yellow*), small branches off the main dendrite shaft that enable learning and memory.

SOURCE: "WHAT HAPPENS TO YOUR BRAIN ON THE WAY TO MARS," BY VIPAN K. PARIHAR ET AL., IN *SCIENCE ADVANCES*, VOL. 1, NO. 4, ARTICLE NO. E1400256; MAY 1, 2015

Illustration by Emily Cooper

more time exploring the new toy or location than objects that have stayed the same, whereas an impaired mouse will spend less time poking around. Such tests have proven to be reliable indicators of various types of hippocampal (memory and learning) and cortical (thinking) functions. We measure an animal's performance through what is called a discrimination index, calculated as the time spent at the novel object or location divided by the total time spent exploring both new and old situations.

Our experiments with the NOR and OiP tasks showed that irradiation significantly lowers a mouse's discrimination index. After six weeks, the performance of mice exposed to these doses (5 and 30 cGy, or centigrays) had dropped by about 90 percent, changes that were surprisingly consistent regardless of dose. Furthermore, very recent tests indicated that these effects last 12, 24 and even 52 weeks after exposure. The results suggest that exposure to similar levels of cosmic radiation may prove problematic to astronauts engaged in critical decision making, problem solving and other vital mission activities.

Scientists are developing drug and dietary countermeasures that could mitigate the worst effects of radiation on the brain. Yet all these efforts are in early stages, and none has the potential to be a cure-all.

TRIMMING THE NEURAL TREE

MY COLLEAGUES AND I also followed up these behavioral tests by imaging brain sections from the irradiated mice. Energetic charged particles traveling through the brain have the potential to profoundly change neuronal circuitry. We wanted to observe any specific physical damage that might correlate with the behavioral changes we found. To do so, we used mice that had been genetically altered so that their brains contained brightly fluorescent neurons that showed up in high-resolution microscopy. We collected a series of fluorescent images of various depths in specific brain areas that we then merged and stitched together to create a three-dimensional representation of the brain.

Our imaging showed significant changes to parts of neurons called dendrites. These are the fingerlike protrusions from the main cell body that receive chemical signals from other neurons (similar protrusions called axons transmit signals). Past studies from our laboratory have found that sparsely ionizing (low LET) x-ray and gamma-ray radiation caused significant reductions in the length, area and branching of dendrites over 10 and 30 days. Collectively we call these changes a reduction of dendritic complexity, a critical parameter that can be compared with the branches of a tree. And our recent study, which we published in 2015 in *Science Advances,* also found that very low doses of charged particles can elicit significant and persistent losses in dendritic complexity.

Moreover, these changes occurred at a specific region of the brain termed the medial prefrontal cortex, a spot known to be involved in memory, which we suspected might be damaged based on our behavioral testing. This is not to say that other regions of the brain were not damaged or that other neural circuitry was not impaired, but our findings demonstrate the benefits of combining behavioral studies with brain imaging to connect the cognitive decline we see with structural changes to specific areas of the brain.

We built on the initial imaging with further high-resolution analysis to search for evidence of other structural alterations such as dendritic spines—small (less than one micron, or a fraction of the width of a human hair)—protrusions from the main shaft of the dendrite that enable learning and memory. If dendrites are branches on a tree, dendritic spines are like the leaves on the branches. Dendritic spines contain the synaptic machinery that allows dendrites to receive neuronal signals, and they come in different shapes that help in various jobs. Our past work with x-rays and protons and more recent work with charged particles have revealed a marked sensitivity of dendritic spines to irradiation. And we found that dendritic spine density, or the number of spines per unit length, significantly decreased after short periods (10 days) and longer times (six weeks) following a mouse's exposure. These serious and persistent effects attest to the capability of charged particles to elicit structural changes of consequence—changes that compromise neurons' ability to mediate neurotransmission by reducing the number of synaptic connections in the brain.

To further underline that the changes in mice's behavior resulted from the changes we found in their neurons, we plotted individual performance against dendritic spine density in the same animal. Our data revealed that as dendritic spine density decreased, so, too, did cognitive ability. Individual animals exhibiting the poorest performance (that is, reduced curiosity or exploration of novelty) also possessed the lowest dendritic spine densities, suggesting that disruption of cognition was at least in part related to reduced numbers of dendritic spines. These data provide the first evidence linking structural damage to the adverse behavioral outcomes observed in animals exposed to cosmic radiation.

These results help to confirm what NASA has suspected for years: radiation may be harmful to astronauts' cognitive performance. Until now, these fears had been based in large part on the clinical literature documenting a range of cognitive effects in patients surviving cranial radiotherapy for treatment of brain cancer. Yet in the past scientists have been hesitant to extrapolate these outcomes to astronauts in space because these are

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different populations being exposed to different types of radiation at different doses. In the clinic, a typical daily dose (2 Gy) would exceed most estimates of the radiation dose incurred during a round-trip to and extended stay on Mars. Interplanetary dose rates are about 0.48 mGy, or milligrays, a day during the roughly 360-day round-trip transit and half that rate during an expected stay of one year or more on Mars (because the planet's bulk blocks the radiation coming from below). Although the total radiation doses used in the clinic are much higher than those found in space, the x-rays and gamma rays typically used to treat tumors are sparsely ionizing (low LET), whereas the charged particles we worry about in space are densely ionizing (high LET). For this reason, we have not been able to make strong comparisons between the outcomes in cancer patients and those we expect in astronauts.

Our work adds new support to the notion that space radiation is harmful to astronauts' brains, but important caveats still persist. Although our experiments used doses of radiation similar to what space travelers would experience, we were unable to deliver those doses at the same rate that astronauts would receive. In space, astronauts would receive the radiation over the course of many months to years, underscoring the protracted nature of cosmic radiation exposure. Because we had only limited time at the accelerator facility, we had to deliver the same dose over a matter of minutes. This large difference in rate might raise doubts about our results because one could suppose that cells would have time to repair and recover when the dose was delivered slowly. In fact, the difference in dose rate is not likely to have a strong effect, because the total dose is low (in other words, particles fly through infrequently), the space particles of most concern are high LET radiation (which produces severe cellular damage that is hard to recover from no matter how quickly it is delivered) and, finally, most areas of the brain cannot generate new neurons easily, which further hinders recovery. And although our findings pertain to rodents, not humans, we have no reason to think a human neuron would respond differently in any significant way to cosmic radiation than our mice's neurons did.

OUR FUTURE IN SPACE?

TO SEND HUMANS OUT into the solar system, we face daunting hurdles. Astronauts will need larger, more powerful rockets than those currently available to reach Mars and other bodies in our solar system, and they will need habitats once they arrive and the ability to use resources at their destination to make water and rocket fuel. We must now add to this list of challenges the need to protect space colonists from radiation, which may prove the hardest barrier to overcome.

The first way we might tackle the problem is via shielding that stops the radiation before it can do any damage—placed either on spacecraft and habitats or in space suits or clothing. At the moment, the only way scientists know how to shield against radiation is with extremely heavy and thick materials such as lead. These do the trick, but they are utterly impractical in space because they are so heavy and would require too much rocket fuel to launch. Efforts are now under way to design advanced shielding materials and engineering controls that can enhance a hull's defense on certain regions of a spacecraft. Astronauts could retreat to these more protected areas during times of elevated solar activity and wear helmets and space suits designed to maximize protection from radiation exposure while spacewalking or even sleeping. It would take a radically better protective material than any that currently exist to make a significant improvement, though.

Scientists are also developing drug and dietary countermeasures that astronauts could take on a regular schedule or after acute radiation exposure (following a major solar storm, for example) that could mitigate the worst effects of radiation on the brain. Antioxidant formulations, for example, have shown promise for limiting some of the damage done to mice exposed to spacelike radiation. Researchers have also made progress in designing chemicals that can bolster brain circuitry to help maintain function after damage has occurred. Yet all these efforts are in early stages, and none has the potential to be a cure-all. The best we can hope is to reduce, rather than eliminate, damage. We must also continue to research cosmic radiation's effects on the brain, as well as the entire body, to elucidate more completely the short- and long-term health risks associated with prolonged exposure.

Our discoveries point to a concern about deep-space travel that has perhaps been underappreciated compared with other dangers. The risk of radiation-induced cancer, for instance, is better known but may actually be of lesser importance because of the long time it takes for most radiogenic cancers to develop. We have shown, however, that even small amounts of cosmic radiation cause neuronal damage and cognitive defects in mice and are very likely to do so in humans as well.

The persistence of these radiation-induced changes is another cause of worry. Scientists have seen no sign that damaged dendritic complexity and spine density can repair themselves after cosmic radiation exposure, and whereas it is premature to refer to such changes as permanent, we have no evidence that neurons recover from this type of injury. Therefore, until researchers find specific interventions that can promote and hasten the healing of the irradiated brain tissue, our best options appear limited to protecting our existing neural circuitry.

Cosmic radiation exposure may well represent one of the more significant obstacles to Mars travel and even more so for longer deep-space missions required to explore more distant worlds. Although some may consider these findings controversial, it remains difficult to dismiss these data and their potential implications for the space program. Does this mean we are forever bound to Earth? Perhaps not. These results may simply represent yet another obstacle that humankind must meet and surpass as we prepare to embark on what may prove to be humanity's most daunting challenge and perhaps even its greatest success. SA

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scientificamerican.com/magazine/sa

LINGUISTICS

THE

Before the smartphone or even Morse code, some rural peoples "spoke" long

WIRELESS COMMUNICATION: In the Greek village of Antia, Kiriakoula Yiannakari demonstrates how to whistle a message to neighbors.

whistled WORD

distance by whistling—a means of communicating that still fascinates linguists

By Julien Meyer

Photographs by Eirini Vourloumis

Julien Meyer is a linguist and bioacoustician at the French National Center for Scientific Research and at the GIPSA-lab in Grenoble, France. His research focuses on phonetics, language cognition, and language and rural communities. He runs the Icon-Eco-Speech project and is a co-founder of the World Whistles Research Association, which documents and safeguards whistled languages.

One spring morning Panagiotis Kefalas

was in the tavern he owned in the tiny Greek village of Antia when he received a call from his friend Kyria Koula. Kefalas was planning to have breakfast at her home some 200 meters from his tavern. The call did not begin with the sounding of a mobile ring tone. Instead it reached directly from Koula's mouth to Kefalas's ears, arriving in the form of a series of high-pitched whistles.

"Welcome, what do you want?" Koula trilled.
Kefalas pursed his lips and whistled back:
"Please, I would like to eat."
"All right," Koula replied.
"I would like scrambled eggs," Kefalas volunteered.

A visitor to Antia would have come away perplexed. The beginning of the first phrase, "welcome" (*kalós irthate* in romanized Greek), sounded like the lewd catcall—"tweet, tweeo"—except that the drawn-out second syllable rose sharply in pitch.

Some accounts contend that the now dying tradition of whistled speech, still maintained by Antia's few dozen residents, served for centuries as the best way for sheep or goat herders there to communicate from one hillside to another. Whistles, after all, carry much farther than shouts and spare the vocal cords. Even today the pensioners of this village at the southern end of Greece's second-largest island, Euboea, sometimes use this efficient pretechnological form of wireless communication from house to house to convey news, gossip or extend a breakfast invitation.

I recorded the conversation between Kefalas and Koula in May 2004. Since the early 2000s I have been studying whistled speech in remote mountains and dense jungle across the globe. In that time, I and my colleagues from diverse institutions have come across many previously undiscovered whistled languages. We have also measured the amazing distances that whistled words can travel and have gained an understanding of how

IN BRIEF

Before electronic communications became a ubiquitous part of people's lives, rural villagers created whistled versions of their native languages to speak from hillside to hillside or even house to house.

Herodotus mentioned whistled languages in the fourth book of his work *The Histories,* but until recently linguists had done little research on the sounds and meanings of this now endangered form of communication.

New investigations have discovered the presence of whistled speech all over the globe. About 70 populations worldwide communicate this way, a far greater number than the dozen or so groups that had been previously identified.

Linguists have tried to promote interest in these languages—and schools in the Canary Islands now teach its local variant. A whistled language represents both a cultural heritage and a way to study how the brain processes information.

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TECHNICAL PROWESS displayed by Antia's Georgia Yiannakari meets with approval from Maria Kefala (*1, in pink*), an expert translator of whistled Greek. Yiannis Tsipas (*2, in middle*) hopes to pass along whistling expertise he learned from his parents—his mother Aristi is at his side—to his son, Vassilis.

blowing air through lips can convey full sentences, as well as how the brains of recipients manage to decode the words.

A SLOW BEGINNING

I ORIGINALLY became interested in these languages almost 20 years ago after reading a 1957 *Scientific American* article about a version called Silbo Gomero, which is still spoken on La Gomera, one of Spain's Canary Islands. I decided I wanted to know more and made it the focus of my doctoral work beginning in 2003.

Back when the article appeared, very few researchers had any interest in studying whistled languages, even though such speech had been known since ancient times; Herodotus mentioned Ethiopian troglodytes who "spoke like bats" in *Melpomene,* the fourth book of his work *The Histories.* By 2003 interest had picked up, but few linguists had done research on the sounds and meanings conveyed by whistled speech, and most studies had investigated only Silbo Gomero.

The term "whistled language" is somewhat of a misnomer. Whistled speech, in fact, is not a separate language or dialect from a native tongue but rather an extension of it. Instead of using the voice to speak the Greek words *Boró na ého omeléta?* ("Can I have scrambled eggs?"), those same words are articulated as whistles. The sounds of the words just undergo a profound shift; they are generated not by the vibrations of the vocal cords but by a compressed stream of air from the mouth that swirls in turbulent vortices at the edge of the lips. Just as in ordinary speech, the whistler's tongue and jaw move to form different words, but the range of movement is more constrained. All that changes is the pitch of the whistle; in contrast, when people speak, the timbre (what distinguishes one sound from another apart from pitch and loudness) may change, too.

In the end, the whistled words conveyed in the village of Antia are still Greek. Linguists sometimes liken a whistle to a whisper, in that both are alternative ways of speaking the same language without using the vibration of the vocal cords. Linguist André Classe, author of the *Scientific American* article that inspired me, termed whistled talk a natural "informational skeleton" in describing its bare-bones nature. He noted that the intelligibility of whistled speech does not always match that of spoken language, but it comes close.

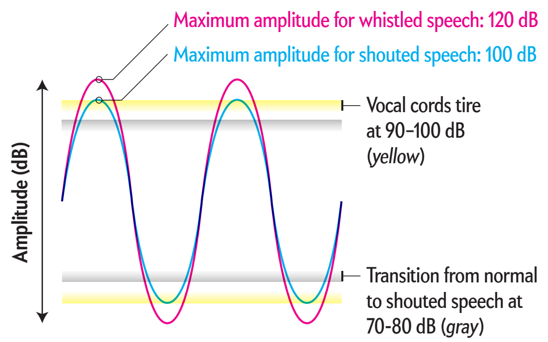
In my early investigations, I found intriguing documents from travelers, colonial functionaries, missionaries and anthropologists that described 12 or so whistled languages. These clues led me to suspect that other whistled counterparts of spoken languages existed around the world.

In the early 2000s I therefore set about with my colleague Laure Dentel to undertake 14 months of fieldwork visiting places where some evidence indicated that this practice still occurred.

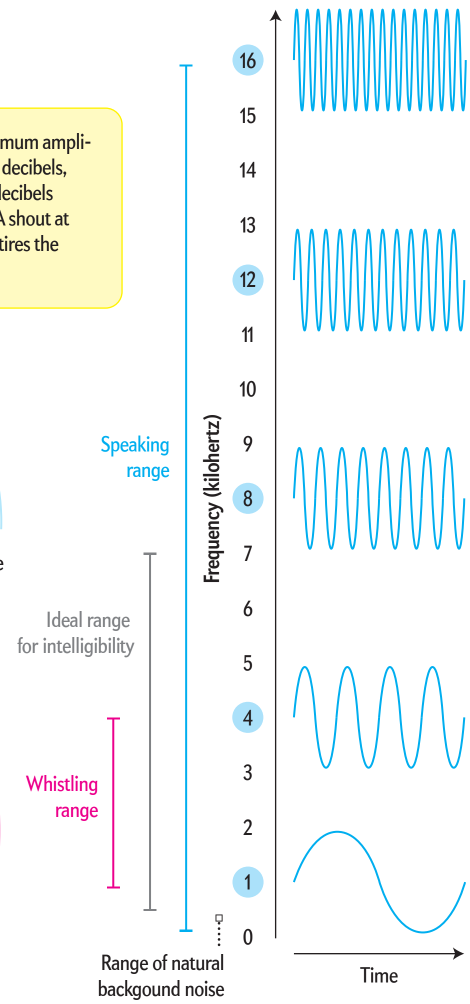
Physics of Pucker and Blow

Whistled speech is an alternative form of a native language—such as Greek, Turkish or Spanish—that conveys words using a compressed stream of air that swirls in tiny vortices at the edge of the lips. A whistled language lacks the harmonics of the voice. Yet the lone, modulated, narrow band of frequencies for representing vowels and consonants in a nontonal language, such as Greek, still fulfills the essential characteristics of a language. It thus allows for nontraditional exploration of the cognitive capacities of the human brain.

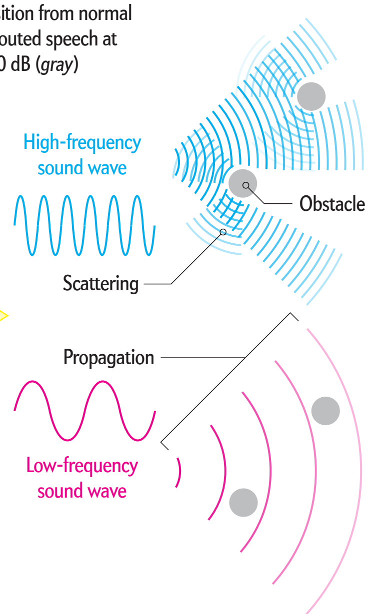
Sound waves generated by whistling fall within the frequency range that engineers and psychologists have found to be optimal for detection by the ear. A whistle is a single-frequency band in this area of spectrum that is easier to detect by the human ear than the complex waves produced by ordinary spoken speech, which span a much broader frequency range.

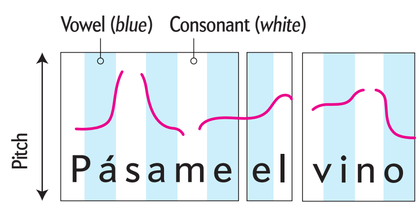


Whistling has a maximum amplitude (volume) of 120 decibels, compared with 100 decibels for shouted speech. A shout at 100 decibels quickly tires the vocal cords.



When sounds propagate under ideal conditions, they lose approximately six decibels each time the distance from the source doubles. Also, an acoustic signal bounces off obstacles, such as the ground and tree trunks. Spoken speech consists of a broad set of frequencies, and a particular band within that range scatters differently from another when coming into contact with a physical object. A whistle, meanwhile, encodes all the linguistic information communicated in a single narrow band. Low-frequency sounds resist scattering by physical barriers, such as dense vegetation, an acoustic property that allows them to propagate farther.





Each type of whistled speech, such as Spanish Silbo of the Canary Islands, has a system of pronouncing vowels and consonants that approximates the spoken one by varying whistled pitch or breaking the flow of air. In this way, most information encoded in vowels and consonants is conveyed through variations in frequency and amplitude. Normal speech also relies on timbre to identify vowels and consonants, which fade at a distance. In contrast, whistlers can clearly enunciate phrases such as "Pass me the wine" and be heard from far away.

The acoustic characteristics of whistling allow the sound to extend up to 10 times farther than shouted speech—a distance that can reach several kilometers in valleys and other areas that transmit sound well.

SOURCE: *WHISTLED LANGUAGES: A WORLDWIDE INQUIRY ON HUMAN WHISTLED SPEECH*, BY JULIEN MEYER. SPRINGER-VERLAG, 2015

Graphic by Amanda Montañez

Subsequently, I joined with a network of colleagues to conduct new field studies all over the world. I have, as part of this effort, documented the whistled speech of the Wayãpi in the Amazon jungle, in collaboration with linguist Elissandra Barros da Silva in Brazil and anthropologist Damien Davy in French Guiana. With Dentel, I have studied the Akha and the Hmong in Southeast Asia and with linguist Rachid Ridouane, the Tamazight Berbers in Morocco's Atlas Mountains. In 2009, moreover, Dentel, linguist Denny Moore and I began a five-year collaboration at the linguistics division of the Emilio Goeldi Museum of Pará in Belém, Brazil. Our job was to chronicle the whistled language of the Gavião people in the Amazonian state of Rondônia.

Our research endeavors have brought to bear the latest tools in linguistics and acoustics and used methods from many fields, among them phonetics, psycholinguistics, bioacoustics and sociolinguistics. We borrowed, for instance, the recording methods bioacousticians use for studying animal communication in the wild because these are well suited for studying whistled communication over large distances.

Our research discovered ways people convey words with whistles. The whistler may pucker the lips, finger whistle, or blow into a leaf or a simple wood flute. Some speakers combine different techniques depending on how far they wish to send a message. Words are constructed from these sounds depending on whether the spoken language from which the whistled one is derived uses changes in tone to convey differences in meaning, such as in Mandarin and Cantonese, or whether tones do little more than let the speaker add stress to a word, as they do in Greek or Spanish. In a tonal language, a whistle's rising pitch mirrors the ascending inflection of the spoken tone. In nontonal languages, however, a whistle's unchanging pitch represents a vowel—an "i" might be communicated with a high-pitched whistle, whereas an "e" might sound at a lower pitch. The whistler forms consonants in either language class by modulating how abruptly the sound is altered when changing from one pitch to another.

CENSUS TAKING

OUR INQUIRY so far has managed to locate about 70 populations who use whistled speech, most hailing from isolated mountainous or densely vegetated locations. That number is just a fraction of the world's 7,000 languages, but it far exceeds the previously recorded tally. In all these places, whistled languages are used mainly, as earlier work suggested, to project messages beyond shouting distances—but they have other uses as well. They can assist in courtship rituals within the confines of a town. They can be used to communicate in a noisy setting or to trade secrets in the presence of nonwhistlers. ("You have to hide because the police are on the way.") And they can help hunters land prey; in the Amazon jungle, animals recognize the human voice but not whistles.

Acoustical analysis of whistling used for long-distance communication shows that, under favorable weather and topographical conditions, a whistle can travel several kilometers. The frequency spans 0.9 to four kilohertz, almost exactly the range determined by telecommunications engineers to be best for picking out accurately the component sounds that make up words. In one experiment we performed in a valley near the French Alps, spoken speech carried 40 meters, shouts 200 meters, whereas a whistle was still intelligible at 700 meters. Though not a whistling record, that measurement demonstrated the relative advantage of whistling under average conditions that included some background noise and a light wind.

For linguists, the study of whistled speech has helped demonstrate the capacity of the human brain to recognize words and sentences in an acoustic signal that carries less information than that produced by the human voice. A given whistle's single frequency lacks the harmonics of the voice. Yet even this lone modulated frequency fulfills the essential requirements of an actual language in clearly communicating information. Whistled speech is therefore an important means to explore the cognitive capacities of our brain to communicate in an untraditional way.

Decades ago bioacoustician René-Guy Busnel, with whom I have collaborated since the beginning of my doctoral work,

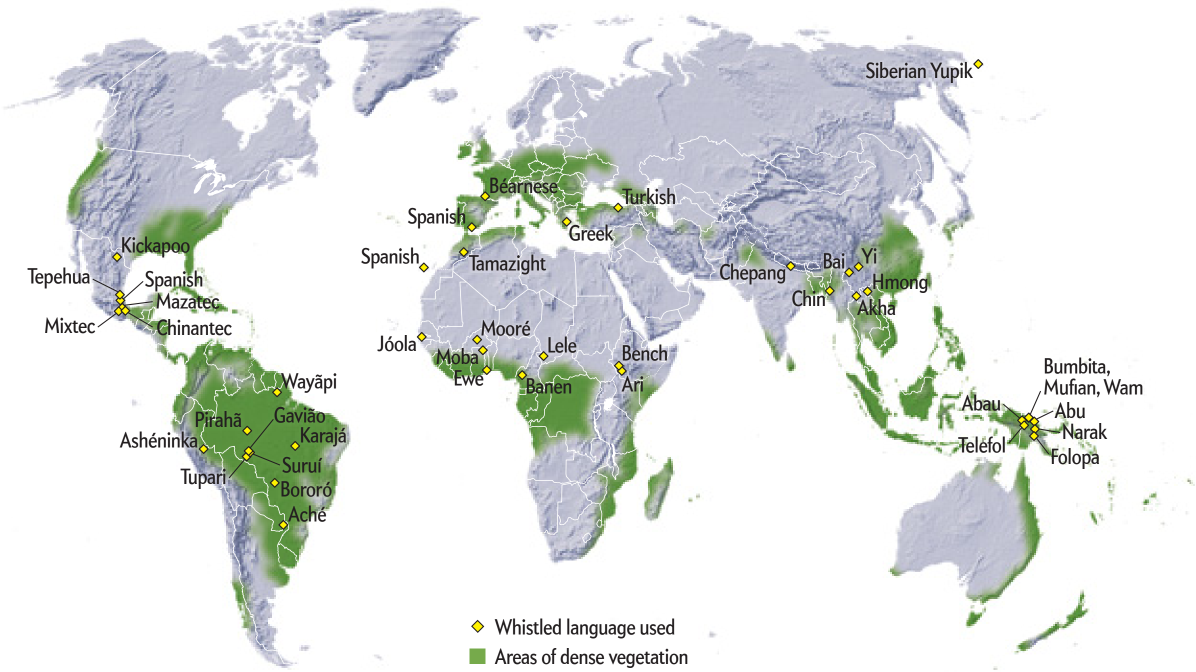
Acoustical analysis of whistles indicates that, under highly favorable conditions, the sound carries over a distance of several kilometers.

conducted a study on whistled speech perception among villagers of Kuşköy in the mountains of northeastern Turkey. Using the whistled form of Turkish known as "the language of the birds," townspeople over short distances could recognize individual words around 70 percent of the time, compared with a 95 percent rate for ordinary spoken words. They could even detect an entire sentence about eight out of 10 times in that situation when people were far enough apart that they could not see one another's faces clearly. This study inspired me to begin another, published in 2013, in which I, along with my colleagues, investigated intelligibility of spoken words as distances increased between a speaker and listener. The results showed that at a separation of 17 meters, word recognition drops to 70 percent. We also found that the best-recognized consonants (sibilants that resemble whistlelike sounds) are still recognized at rates above 90 percent up to 33 meters away. Combined with Busnel's work on whistled Turkish, these results suggest whistled speech is more efficient than ordinary spoken speech when interlocutors are communicating across medium distances of 20 to 30 meters.

Also in the realm of linguistics, I was curious about how readily a person can learn some of the rudiments of whistled speech. Traditionally, the skill is taught shortly after a child learns to talk, but we decided to investigate the initial steps of whistled-speech learning in adults. I asked 40 university French- and Spanish-

Where the World Speaks in Whistles

In the past 15 years the number of known whistled languages has expanded to about 70 from the dozen or so initially identified by anthropologists, missionaries, travelers, and the like. The ones that have been studied or recorded are noted on the map. As research continues, more whistled languages will be discovered, provided that their traditional ways of living are not threatened by modernity. Often they are used to communicate over long distances in mountainous and forested areas.



speaking students to listen to Silbo Gomero. We found that the students readily distinguished an obvious component of any Spanish whistled word—the vowels "a," "e," "i" or "o" ("u" is whistled as "o" in Silbo Gomero)—and that the Spanish students were a little more accurate than the French ones. Both groups of students categorized correctly the vowels far above chance, though not as well as a trained Silbo speaker.

LEFT *AND* RIGHT BRAIN

THE NEUROBIOLOGY OF WHISTLING is one area that remains largely unexplored. Researchers have only begun to observe what happens in the brain's language centers when a person speaks via whistles. But we have made some progress. One 2005 study published in *Nature* by Manuel Carreiras, then at the University of La Laguna on Tenerife in the Canary Islands, and his colleagues reported brain areas underlying language comprehension—the temporal regions of the left hemisphere—are activated in well-trained whistlers when they listen to Silbo Gomero. The finding implied that these same known language-related areas could process words from a simple auditory input consisting of changes in pitch (akin to a musical melody) in experienced whistlers, though not in people unfamiliar with whistled speech.

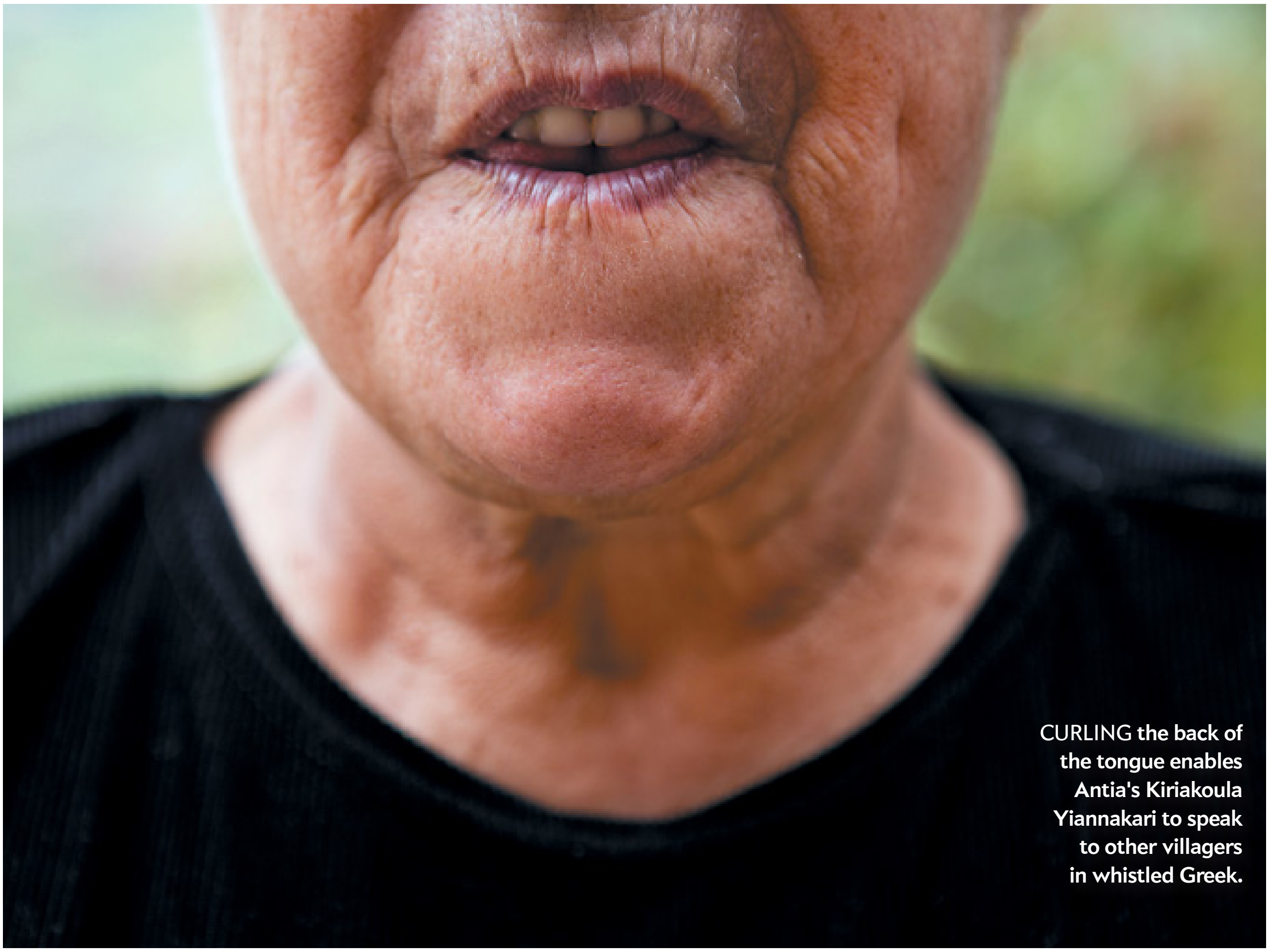
Another investigator wanted to know whether the concentration of brain activity in the left hemisphere was the whole story. Onur Güntürkün of Ruhr University Bochum in Germany recruited speakers of the Turkish whistled language to test the conventional notion that the brain's left hemisphere is where most language processing occurs. Earlier studies had shown that the left hemisphere is, in fact, the dominant language center for both tonal and atonal tongues as well as for nonvocalized click and sign languages. Güntürkün was interested in learning

Recent studies reveal that whistled languages can expand our understanding of the way the brain processes auditory information.

SOURCE: *WHISTLED LANGUAGES: A WORLDWIDE INQUIRY ON HUMAN WHISTLED SPEECH.* BY JULIEN MEYER. SPRINGER-VERLAG, 2015

Map by Mapping Specialists

SCIENTIFIC AMERICAN ONLINE Listen to whistled Greek at ScientificAmerican.com/feb2017/whistler



CURLING the back of the tongue enables Antia's Kiriakoula Yiannakari to speak to other villagers in whistled Greek.

how much the right hemisphere—associated with the processing of melody and pitch—would also be recruited for a whistled language. He and his colleagues reported in 2015 in *Current Biology* that townspeople from Kuşköy, who were given simple hearing tests, used both hemispheres almost equally when listening to whistled syllables but mostly the left one when they heard vocalized spoken syllables. This result needs further confirmation in other whistled languages but provides a challenge to the prevailing idea that the left hemisphere is dominant in language comprehension.

These studies demonstrate that whistled languages can help expand knowledge of the way the brain processes information. I currently promote these research efforts as a member of two organizations. The World Whistles Research Association has been in place since 2002, and a new endeavor on whistled speech was launched in 2015 by my laboratory (GIPSA-lab) at the French National Center for Scientific Research.

Scientists studying whistled languages may also receive a boost from nascent efforts to preserve these unique forms of communication as part of the cultural heritage of various peoples. The Canary Islands were ahead of the pack in that regard. In 1999 they made teaching of Silbo Gomero mandatory in primary schools on the island of La Gomera. They also set up a formal government program to develop whistling teachers. The desire to revive Silbo has since inspired a series of initiatives—for instance, the Cultural and Research Association of Silbo Canario Hautacuperche, an organization that provides whistled-speech courses, even contributed by launching an app called Yo Silbo to train people by listening to correctly whistled sentences.

If similar efforts take hold, whistling for your supper could become more than a saying. It would preserve a form of expression that is giving new insight into how simple high-pitched tones can be molded to communicate complex thought. SA

MORE TO EXPLORE

Typology and Acoustic Strategies of Whistled Languages: Phonetic Comparison and Perceptual Cues of Whistled Vowels. Julien Meyer in *Journal of the International Phonetic Association,* Vol. 38, No. 1, pages 69–94; April 2008.

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Whistled Turkish Alters Language Asymmetries. Onur Güntürkün et al. in *Current Biology,* Vol. 25, No. 16, pages R706–R708; August 17, 2015.

World Whistles Research Association: **www.theworldwhistles.org**

FROM OUR ARCHIVES

The Whistled Language of La Gomera. André Classe; April 1957.

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scientificamerican.com/magazine/sa

INSIDE JOB: Scans for thyroid or bone cancer, such as this one, rely on a rare isotope called technetium 99m.

HEALTH

BLIND MEDICINE

Millions of patients depend on a rare radioactive form of one element to scan them for disease. But the old nuclear reactors that make it are shutting down

By Mark Peplow

The man with radioactive atoms flowing through his veins seems calm. He moves onto a gurney and lies still as it slides into a humming, doughnut-shaped scanner at Vancouver General Hospital. His foot hurts—a lot—and the machine takes sharp 3-D snapshots of bones and soft tissue within by imaging these atoms, their radiation shining brightest where there is increased blood flow to the injury.

This kind of bright beacon does not just illuminate feet. More than 30 million times a year, all over the world, scans that use these atoms track the irregular beat of damaged hearts, uncover deadly cancers and explore brains devastated by stroke. These pictures rely on an obscure isotope called technetium 99m, used in an imaging process called single-photon emission computed tomography. The injected technetium gives doctors an unmatched window into the body, allowing them to pinpoint damage or disease so they can save patients' lives. These images can show finer detail than other tests, and the radiation dose is extremely low and safe.

Now these precious pictures are endangered. The radioactive atoms coursing through this patient's foot got their start at an old nuclear reactor thousands of kilometers away in Chalk River, Ontario. On October 31, 2016, that reactor stopped making the source material for the isotope. At that moment North America was left with no domestic source of this vital medical tool, and 20 percent of global production disappeared. Chalk River will shut down completely in a few years. And the problem gets worse.

Very nearly all of the world supply comes from just six research reactors. Four of them are more than 50 years old and increasingly prone to breakdowns. Two reactors, in Belgium and the Netherlands, now account for half of global capacity and will be shuttered in the coming decade. New nuclear plants are planned but could take more than a decade to complete. Last September the U.S. National Academies of Sciences, Engineering, and Medicine rang a loud alarm with a report saying there was a "substantial" chance of shortages in the near future.

Doctors are worried. "It's something we need on a daily basis,"

IN BRIEF

An obscure radioactive atom, technetium 99m, is essential for lifesaving medical scans.

The world supply is running out as aging nuclear reactors that produce material to make this atom shut down.

Researchers are racing to develop new methods using particle accelerators and other machines to fill the gap.

SCIENCE SOURCE

Science journalist **Mark Peplow** wrote about nanotechnology in medicine in the April 2015 issue of *Scientific American.*

says Eric Turcotte, a nuclear medicine specialist at the University of Sherbrooke in Quebec. These tests are especially useful for detecting bone cancer or fractures—the foot patient's physicians were looking for small breaks—and for revealing blockages in a heart patient's arteries. They are often given to people with chest pain or other signs of blood vessel disease. Other techniques produce blurrier, less exact images or use higher doses of radiation that pose a greater danger of harm. Benjamin Chow, a cardiologist at the University of Ottawa Heart Institute, says that a shortage would force doctors to fall back on less accurate methods, increasing patient risks, or to skip the tests altogether.

Worse, cutting back to just a few production sites creates an easily broken supply chain. Almost all of the isotope decays in a day and cannot be stockpiled. Each short-lived dose for a patient has to be freshly milked from a container holding its source, a longer-lasting isotope called molybdenum 99. Supplies of that material need to be flown in every few days from the reactors that make it, halfway around the world. Bad weather and canceled flights could mean no scans. "If an airport is closed, just think how vulnerable we are," frets François Bénard, a clinician-scientist at the BC Cancer Agency in British Columbia.

The isotope's production cycle raises another problem: nuclear terrorism. To create molybdenum 99, most reactors use weapons-grade highly enriched uranium (HEU). There is a global push to stop using HEU by 2020 because dangerous people and rogue states want to steal it. But converting reactors to use low-enriched uranium (LEU) means more downtime, and LEU reactors ultimately produce less molybdenum 99.

To avert this looming crisis, researchers in the U.S. and Canada have been racing to develop radically new technologies to produce molybdenum 99 and technetium 99m without nuclear reactors, instead using more nimble particle accelerators and other machines. Not only could these techniques avoid shortages, they could also be cheaper and produce much less radioactive waste. Now, with global capacity dropping sharply, the researchers are about to find out if their alternatives are up to the challenge.

COMING UP SHORT

DOCTORS ALREADY HAVE BITTER EXPERIENCE with what happens when molybdenum 99 runs out. Back in 2009 and 2010, both the Canadian and Dutch reactors were off-line for extended periods, causing a global shortage that left doctors scrambling to find alternative diagnostic tests. "The crisis in 2009 was a wake-up call for everyone," says Sally Schwarz, president of the Society of Nuclear Medicine and Molecular Imaging. "Diagnostic tests couldn't be performed, and patients suffered. We don't want to be in that position again."

One common fallback for a technetium 99m heart test, for instance, uses another radioisotope called thallium 201. But this isotope produces blurrier images and doubles the patient's radiation dose, says heart-imaging specialist Venkatesh L. Murthy of the University of Michigan. And other, nonradioactive methods, such as echocardiography, are not as precise. Technetium 99m hits a sweet spot between resolution, safety and cost, he says.

Sobered by the effects of the shortfall, the Canadian government soon afterward began the $45-million Isotope Technology Acceleration Program (ITAP) to develop alternative ways to make technetium 99m. Its leading project may be ready to go online by the end of this year.

Instead of an enormous reactor plant, the technology uses a small particle accelerator called a cyclotron, which can fit in the basement of a hospital. The cyclotron smashes protons into a target made of a different isotope, molybdenum 100, and the collision produces technetium 99m at the site. The isotope's short half-life means that a single cyclotron can serve only a limited area. But most of Canada's big cities already host similar machines, so it should be possible to roll out the solution across the whole country, says Paul Schaffer, an associate lab director and former head of the nuclear medicine division at Canada's flagship cyclotron center, TRIUMF, which developed the method. TRIUMF, located in Vancouver, ran pilot tests to demonstrate that it can make enough technetium 99m during a six-hour cyclotron run to meet the needs—about 500 scans a day—of the province of British Columbia, which has a population of nearly five million.

Currently the two-meter-wide cyclotron sits in a vault behind a thick steel door at the Vancouver facility of the BC Cancer Agency. Two thin metal tubes jut from the machine, carrying beams of protons traveling at about one-fifth the speed of light. At the other end lies the target: a thin, flat plate about 10 centimeters long, with a coating of molybdenum 100, housed in an aluminum cylinder. The plate is bombarded for six hours to transform some of the molybdenum 100 into technetium 99m. Then it is shot through an air-pressure tube into a lead-lined work chamber called a hot cell in another room, where operators separate and purify the technetium 99m. The result is a small vial of clear liquid containing enough of the isotope for hundreds of tests.

Vancouver General Hospital and the cancer agency are just wrapping up a clinical trial using this technetium in real tests on patients. The generation process generally starts in the early hours of the morning, and patients can be booked for injections starting at 1 P.M. The trial results so far indicate that the cyclotron technetium is just as safe and effective as the isotopes made with the molybdenum 99 containers.

TRIUMF and other ITAP partners launched a company last year to supply the technology to other cyclotrons. Already about 500 medical cyclotrons worldwide have sufficiently powerful beams to make technetium 99m in this way, in addition to their current tasks such as producing isotopes for positron-emission tomography scans. That existing base is a big advantage, Schaffer says: a new medical cyclotron might have a $5-million price tag, but it costs a tenth of that figure to retrofit an existing machine. In 2014 the British Nuclear Medicine Society recommended this approach as the most suitable way to supply technetium 99m, and Schaffer reckons that between 12 and 24 cyclotrons could meet Canada's entire needs.

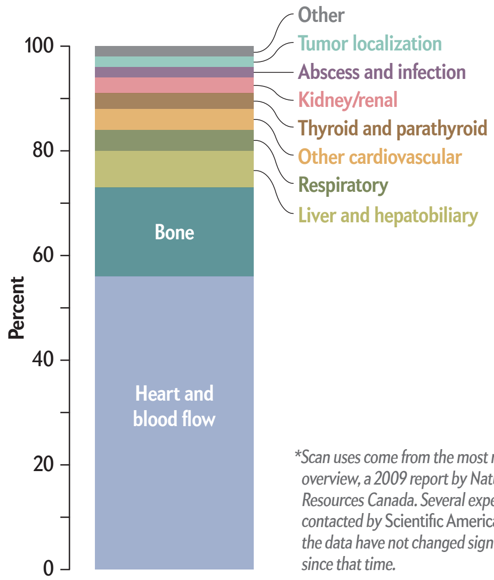
GENERATING ADVANCES

SOUTH OF THE CANADIAN BORDER, in the U.S., however, cyclotrons are not generating as much enthusiasm—or technetium. The trouble is that the nation's hospitals were among the very first to build medical cyclotrons, and these older models cannot

DIAGNOSTIC TESTS

Vital Isotope Uses

The isotope technetium 99m is used in about 30 million medical scans every year. More than half of them are tests for potentially fatal heart and blood vessel problems. Others detect bone cancer, kidney disease, and more.*



*Scan uses come from the most recent overview, a 2009 report by Natural Resources Canada. Several experts contacted by *Scientific American* say the data have not changed significantly since that time.

SOURCE: NATURAL RESOURCES CANADA, PRESENTED TO HOUSE OF COMMONS STANDING COMMITTEE ON NATURAL RESOURCES, JUNE 2, 2009

reach the higher beam energy that is now needed, Schaffer says.

Instead the U.S. Department of Energy's National Nuclear Security Administration is backing companies with different machines. One firm, NorthStar Medical Radioisotopes in Madison, Wis., hopes to use an electron linear accelerator (LINAC) to generate high-energy x-rays. These can knock a neutron out of molybdenum 100, transforming it into molybdenum 99, which will decay into technetium. LINACs are easier to license than nuclear reactors, cost less than cyclotrons and can essentially be bought "off the shelf," says Carl Ross, a retired physicist who worked on linear accelerators at Canada's National Research Council. (Canadian Isotope Innovations, spun out of research funded under ITAP, is taking a similar approach but is not as far along.)

Yet for all their advantages, standard linear accelerators produce lower concentrations of molybdenum 99 than reactors do. So NorthStar has developed a completely new system to separate technetium 99m from the mixture of molybdenum isotopes that comes out of its LINACs. Dubbed "RadioGenix," it pumps the mixture through a column of resin that absorbs only technetium. The molybdenum isotopes can then be recycled for another production run, and the pure technetium can be stripped from the column with a saline wash. The company hopes the system will be approved for clinical use this year.

Another solution, perhaps the most radical approach, comes from SHINE Medical Technologies in Monona, Wis., which wants to make molybdenum 99 by bombarding a liquid brew of LEU with neutrons. Those come from a LINAC that smashes deuterium into tritium. Both are heavy isotopes of hydrogen, and they fuse to form another element, helium. This merger releases a neutron. Those neutrons can then trigger fission reactions in the LEU target, forming molybdenum 99. The company says that the process produces concentrations of molybdenum 99 that are compatible with existing systems for transporting the isotope and separating, or milking, technetium 99m from it. (Because of the milking process, these canisters are whimsically dubbed "moly cows.") In February 2016 SHINE got approval from the U.S. Nuclear Regulatory Commission to build its production facility, and it hopes to begin supplying by 2020.

PRICE POINTS

BUT SMART TECHNOLOGY is no guarantee of success. Costs will play a major role. "You need to make the product at a competitive price for it to be accepted by hospitals," Bénard says.

Using current methods, technetium 99m costs about $20 to $25 per dose in North America. That is much lower than the true cost of production, in part because governments paid a large share for nuclear reactor fuel, waste handling and the original price of building the reactors themselves. "We became addicted to the fact that governments were subsidizing their operation," Schaffer says. "That model is unsustainable."

With the new technology and more private, domestic control over the supply chain, producers and governments plan to price technetium 99m to cover the expenses of maintaining the entire chain. Hospitals in British Columbia are bracing for a 40 percent price rise in the next few years, Schaffer says.

Pricing based on full-cost recovery could help the start-ups get off the ground and stay there. But they also face conflicting market forecasts. On one hand, aging populations in developed countries should increase demand for the heart tests that technetium 99m excels at, and the Chinese market is growing rapidly.

On the other hand, in recent years demand for technetium 99m has actually declined in many countries, according to the Organisation for Economic Co-operation and Development (OECD). The reason? The shortages of 2009–2010 spurred hospitals to reduce the amount of technetium in each dose. Image quality remained high because of smarter imaging software. As a result, the OECD projects that if new reactors and new methods come online there could be a glut and lower prices by 2021.

But many in the field remain unconvinced that replacement reactor capacity will arrive on schedule. "If we just rely on reactors, we'll end up in trouble again," says the BC Cancer Agency's Bénard. To keep the images coming, he believes, new technologies must come into the picture. SA

MORE TO EXPLORE

Lessons from the Tc-99m Shortage: Implications of Substituting Tl-201 for Tc-99m Single-Photon Emission Computed Tomography. Gary R. Small et al. in *Circulation: Cardiovascular Imaging,* Vol. 6, No. 5, pages 683–691; September 2013.

Cardiac Stress Testing and the Radiotracer Supply Chain: Nuclear Freeze. Venkatesh L. Murthy et al. in *JAMA Cardiology,* Vol. 1, No. 5, pages 616–617; August 1, 2016.

Molybdenum-99 for Medical Imaging. National Academies of Sciences, Engineering, and Medicine. National Academies Press, 2016.

FROM OUR ARCHIVES

Positron-Emission Tomography. Michel M. Ter-Pogossian, Marcus E. Raichle and Burton E. Sobel; October 1980.

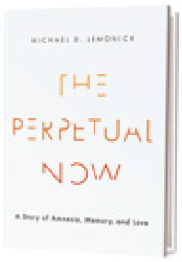
scientificamerican.com/magazine/sa

Graphic by Amanda Montañez

By Clara Moskowitz

MORE TO EXPLORE
FOR AN INTERVIEW WITH AUTHOR SCHUTT, VISIT
scientificamerican.com/feb2017/recommended

The Perpetual Now:
A Story of Amnesia, Memory, and Love
by Michael D. Lemonick.
Doubleday, 2017 ($27.95)



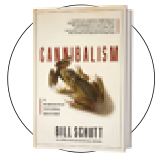
ARTIST Lonnie Sue Johnson created this illustration for the *New York Times* before her injury.

Lemonick, an editor at *Scientific American,* delivers a finely observed profile of Lonni Sue Johnson, an artist and musician who developed a rare viral infection of the brain that destroyed much of her capacity to recall the past and form new memories. Amazingly, the virus left many other parts of her cognition intact, including her speech, exuberant personality, and ability to write, draw and play the viola. Because she was more accomplished before her illness than any other amnesiac previously studied, Johnson has offered scientists an unparalleled opportunity to learn how memories are made, stored and retrieved—for instance, after becoming sick, she failed to recognize many well-known works of art but recalled in perfect detail how to paint a watercolor and describe her technique. Lemonick details Johnson's willing participation in this research, writing of how she lightened up sessions in the functional MRI machine by singing to herself. He also introduces readers to Johnson's mother and sister and the community of neighbors and artists in her adopted town of Cooperstown, N.Y., who rallied to her aid, such as by playing music for her in the hospital and ensuring that she could continue making art. —*Christine Gorman*

Testosterone Rex:
Myths of Sex, Science, and Society
by Cordelia Fine. W. W. Norton, 2017 ($26.95)

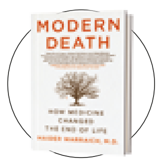
The hormone testosterone has taken on almost mythical status in popular consciousness, often credited with outlandish feats, such as causing the 2008 financial collapse (supposedly because it drove male-dominated Wall Street to extreme levels of risky behavior). But psychology professor Fine demonstrates that testosterone "is neither the king nor the king maker—the potent, hormonal essence of competitive, risk-taking masculinity—it's often assumed to be." She canvasses the history of research showing that testosterone's effects are less powerful and predictable than commonly thought and that male and female brains are not nearly as divergent as popularly believed. Further, she convincingly and entertainingly demonstrates that, despite stereotypes, such characteristics as risk-taking, competitiveness and nurturing are not "essential" to one sex over the other and cannot be blamed for the lack of equality between males and females in contemporary society.

Cannibalism:
A Perfectly Natural History
by Bill Schutt. Illustrations by Patricia J. Wynne.
Algonquin Books, 2017 (26.95)



Plenty of animals cannibalize one another as part of mating or child rearing or for simple hunger. That includes biology professor Schutt, who ate cooked placenta osso buco as research for this humorous history. The story's appetizer is an exploration of cannibalism in nature, such as the practices of fish parents that swallow mouthfuls of their own eggs or of spiders that eat their partner's abdomen while copulating. Humans are the book's main course. Sometimes we consume one another under great duress, such as the famous Donner party, the 19th-century pioneers who ate their dead after a snowstorm marooned them in the Sierra Nevada mountain range. We even eat other humans for supposed medicinal benefits: pharmacies sold powdered ancient Egyptian mummies as recently as 1908; today some mothers consume their own placenta for unproved health benefits. The book is enhanced by the charming drawings of Pat Wynne, whose art has also graced the pages of this magazine. —*Ryan F. Mandelbaum*

Modern Death:
How Medicine Changed the End of Life
by Haider Warraich.
St. Martin's Press, 2017 ($26.99)



Medical advances over the past century have given doctors unprecedented tools to stave off death, pushing life expectancies longer and longer. But the more we learn about dying and how to prevent it, the blurrier the line looks between life and death, physician Warraich writes: "These days we can't even be sure if someone is alive or dead without getting a battery of tests." Both research and human experience would benefit if we could talk more openly about death, he argues. To aid that goal, Warraich demystifies what is known and unknown about how cells and bodies die, while sensitively grappling with the changing cultural landscape surrounding the end of life, including patients who tweet and share the details of their decline on social media. His story is filled with compassionate accounts of the different ways he has witnessed people meet death in the modern age.

Michael Shermer is publisher of *Skeptic* magazine (www.skeptic.com). His book *The Moral Arc* (Henry Holt, 2015) is out in paperback. Follow him on Twitter @michaelshermer

Imagine No Universe

Science contemplates the incomprehensible

By Michael Shermer

Imagine nothing. Go ahead. What do you see? I picture dark empty space devoid of galaxies, stars and planets. But not only would there no matter, there would be no space or time either. Not even darkness. And no sentient life to observe the nothingness. Just … nothing. Picture that. You can't.

Here we face the ultimate question: Why is there something rather than nothing? I have compiled several responses from a number of sources, including a 2013 book by John Leslie and Robert Lawrence Kuhn entitled *The Mystery of Existence* (Wiley-Blackwell) and Lawrence M. Krauss's 2017 book *The Greatest Story Ever Told—So Far* (Atria Books).

Nothing is nonsensical. It is impossible to conceptualize nothing—not only no space, time, matter, energy, light, darkness or conscious beings to perceive the nothingness but not even nothingness. In this sense, the question is literally inconceivable.

Nothing is something. It is a logical fallacy to talk about "nothing" as if it were a "something" that ceases to exist. Here we bump up against the problem of defining what we mean by "nothing" and the restrictions that language imposes on the problem. The very acting of talking about "nothing" makes it a "something." Otherwise, what are we talking about?

Nothing would include God's nonexistence. In Leslie and Kuhn's taxonomy of "nothings," they list what categories of things might be included in "something" that would be negated by "nothing": physical, mental, platonic, spiritual and God. If by "nothing" is meant no physical objects or matter of any kind, for example, there can still be energy from which matter may arise by natural forces guided by the laws of nature. Physicists, for example, talk about empty space as seething with virtual particles, from which particle-antiparticle pairs come into existence as a consequence of the uncertainty principle of quantum physics. From this "nothingness," universes may "pop" into existence.

Nothing excludes creation *ex nihilo*. If by "nothing" is meant that there is no physical, mental, platonic or nonphysical entity of any kind, then there can be no God or gods, which means that there cannot be anything outside of nothing from which to create something. This negates the Christian theologian argument that God created the universe *ex nihilo,* or "out of nothing," based on the English translation of Genesis 1:1 that "in the beginning God created the heavens and the earth." This is misleading. Recent scholarship has suggested that the Hebrew word for "creation" in Genesis 1:1 is *bara* (ברא)—a verb that more accurately translated means to "separate" or "divide." Genesis 1:1 should read, "In the beginning God *separated* the heavens and the earth." Separated from *what* is not indicated.

Nothing is unstable; something is stable. Asking why there is something rather than nothing presumes "nothing" is the natural state of things out of which "something" needs an explanation. Maybe "something" is the natural state of things, and "nothing" would be the mystery to be solved. In his sweeping narrative, *The Greatest Story Ever Told—So Far,* a sequel to his 2012 book *A Universe from Nothing,* Krauss notes that "Einstein was one of the first physicists to demonstrate that the classical notion of causation begins to break down at the quantum realm." Although many physicists objected to the idea of something coming from nothing, he observes that "this is precisely what happens with the light you are using to read this page. Electrons in hot atoms emit photons—photons that didn't exist before they were emitted—which are emitted spontaneously and without specific cause. Why is it that we have grown at least somewhat comfortable with the idea that photons can be created from nothing without cause, but not whole universes?"

One answer has to do with our discomfort with the Copernican principle, which holds that we are not special. We prefer religious and anthropic explanations that the universe was created and fine-tuned for us because they put humans right back in the center of the cosmos anthropocentrically—it is all about *us.* But 500 years of scientific discoveries have revealed that it isn't about us. From this fact, we may gain purchase on a perspective that engages both the religious and scientific impulse toward a sense of awe one gains from contemplating nothing. SA

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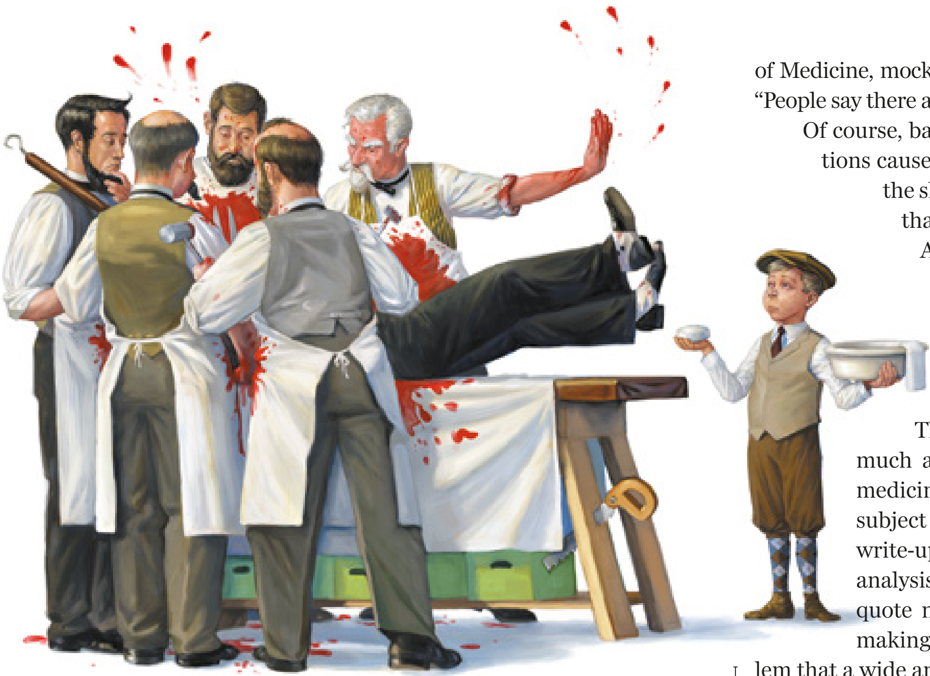
Illustration by Izhar Cohen

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.



None So Blind

Disregarding new scientific information can be deadly

By Steve Mirsky

On July 2, 1881, Charles Guiteau shot President James Garfield in the back. On September 19, 1881, Garfield died, with a bullet still lodged in fatty tissue behind his pancreas. At his trial, Guiteau denied killing the president. "Garfield died from malpractice," the gunman said. His point was made incredibly moot when he was executed by hanging. But he'd made a decent argument.

Historian David Oshinsky discusses Garfield's medical care in his fascinating new book *Bellevue: Three Centuries of Medicine and Mayhem at America's Most Storied Hospital:* "Had the responding physicians ... done nothing more than make Garfield comfortable," Oshinsky writes, "he almost certainly would have survived. Instead they searched clumsily for the bullet, inserting unwashed fingers and filthy probes into the open wound."

Two days after the shooting, experts, including Frank Hamilton, a surgeon in his late 60s from Bellevue, examined the president, "without pausing to wash their hands or clean their instruments," Oshinsky notes. Hamilton's age was a factor, with the old guard less receptive to newfangled ideas about handwashing and instrument cleaning.

As fellow Bellevue veteran Alfred Loomis put it at the time, according to Oshinsky, "The [germ] theory, which so recently has occupied medical men, especially in Germany, is rapidly being disproved, and consequently is rapidly being abandoned." Loomis, respected enough to also serve as president of the New York Academy of Medicine, mockingly told an audience of his fellow physicians, "People say there are bacteria in the air, but I cannot see them."

Of course, bacteria don't care if you believe in them. Infections caused Garfield to lose almost 100 pounds between the shooting and his death, and his autopsy showed that a good part of what was left of him was pus.

Adding insult to literal injury, Hamilton sent Congress a bill for what we'll call his services in the sum of $25,000—equivalent to about $600,000 today. Congress approved a $5,000 payment, which is still about $120,000 in modern money for not washing your hands.

The Garfield section of Oshinsky's book (as much a history of New York City and of American medicine as it is of Bellevue) made me think of the subject considered in this space last month. That write-up dealt with the revolution in the statistical analysis of baseball. But the larger issue was, if I may quote myself, "information availability and decision making in baseball as a microcosm of the larger problem that a wide array of human enterprises face: insisting on remaining stupid when becoming smarter is an option."

Which, speaking of Congress, brings us to the House of Representatives Committee on Science, Space, and Technology. On December 1 the committee's Twitter account announced that global temperatures were in fact plummeting and that what they called "climate alarmists" had clammed up (perhaps in their rapidly acidifying ocean habitat).

The committee's source for this welcome info was Breitbart News. If you were lucky enough to spend the 2016 presidential election campaign in a medically induced coma, Breitbart regularly produces the other stuff that comes out of a cow's backside besides the greenhouse gas methane.

The committee chair, Representative Lamar Smith of Texas, has harassed legitimate climate scientists and does not buy global climate change. He easily could buy it, given that the fossil-fuel industry has given him more than $600,000. That's not just dirty money—it's full of soot.

According to Oshinsky, Loomis finally accepted germ theory when Robert Koch showed that the tuberculosis bacterium was indeed visible, if you used a microscope. Climate change is also obvious if you use worldwide surveillance, including that recorded by NASA satellites. But as I write these words, the new presidential administration is planning to do away with NASA's Earth observation mission because—why?—it's become political. (Don't think about that reasoning too much, or the smoke coming from your ears will further contribute to the greenhouse effect.)

This move is like Loomis gouging his eyes out rather than seeing through the microscope. And we insist on staying stupid when becoming smarter is an option. 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

1967 Gene Therapy

"Some biologists have wondered if it might someday be possible to alter the genetic material of a human being, for example, to supply a deleted gene and thereby remedy some metabolic deficiency. How would one introduce the desired genetic information? One possibility that has now received some preliminary experimental support would be to administer a harmless virus that bears the required gene. The Shope papilloma virus, which causes tumors in rabbits, also induces the synthesis of a distinctive form of the enzyme arginase. The question arose whether the same effect might be obtained in human beings, but one may not infect people with animal viruses for experimental purposes. Stanfield Rogers of the Oak Ridge National Laboratory got at the question indirectly: the blood of people who had worked with, and therefore been exposed to, the Shope virus was found to be carrying 'virus information.' The Shope virus, Rogers suggests, is a harmless 'passenger' virus in these people. It is possible that there are other such viruses."

1917 Mosquito Killers

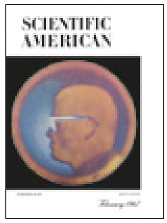
"A report to the French Academy of Sciences tells of a unique experiment in combating a mosquito plague. Myriads of mosquitoes infest the rice plantations of Madagascar, and it occurred to Dr. Legendre to fight the marsh fever [malaria] caused by the bite of the mosquito by introducing into the watercourses the 'Cyprin' or red fish [goldfish], which is a glutton as a devourer of mosquitoes. Dr. Legendre introduced 500 of these fishes into the streams of one district, and in five months they had multiplied and destroyed all the mosquitoes. The natives have found the red fish very much to their liking, and they are proving an important addition to their stock of food."

War Clouds Looming

"If we are drawn into the world war, we may well prove to be the decisive factor; even though we land not a single soldier upon European soil. Excellent though it may be in morale and in its all-round military efficiency, our army would be lost amid the embattled millions of Europe; and our battleships would be superfluous in the North Sea. But the moment our enormous financial resources and our vast potentiality for the manufacture of guns, powder and shells were lined up behind the allied armies, the ultimate overthrow of the Central Powers would be as certain as the rise and setting of the sun."

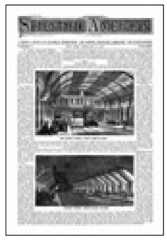
1867 National Academy of Design

"Forty-two years ago the resident artists of the city of New York united in forming a 'Drawing Association,' having for their object the study of art and social intercourse among the members. In 1826 they adopted the name of the National Academy of Design. An important era in the history of the organization witnessed the completion of the magnificent edifice located on 23rd Street, corner of Fourth Avenue [now called Park Avenue South], and represented in the accompanying engraving [*see illustration*]. The style of architecture may be designated the 'revived Gothic,' embracing the features of the different schools of architecture of the Middle Ages, which are most appropriate for our buildings of modern date. The building was designed by Mr. Peter Bonnett Wight of this city." *The academy sold the building in 1899, and it was torn down.*



1967

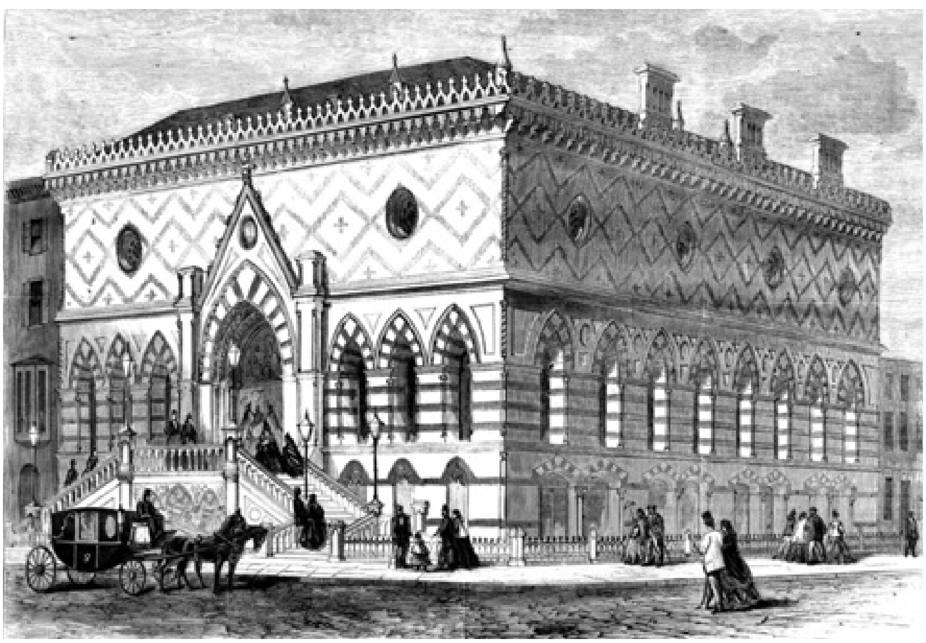
1917



1867

Words, Words, Words

"Prof. Max Müller quotes the statement of a clergyman that some of the laborers in his parish had not 300 words in their vocabulary. A well-educated person seldom uses more than about 3,000 or 4,000 words in actual conversation. Shakespeare, who displayed a greater variety of expression than probably any other writer in any language, produced all his plays with about 15,000 words."



Gothic Revival exhibition and classroom space built for the National Academy of Design, shown in 1867. Other images of grand architecture from 1867 are at **www.ScientificAmerican.com/feb2017/architecture**

SCIENTIFIC AMERICAN, VOL. XVI, NO. 7; FEBRUARY 16, 1867

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Novel Math

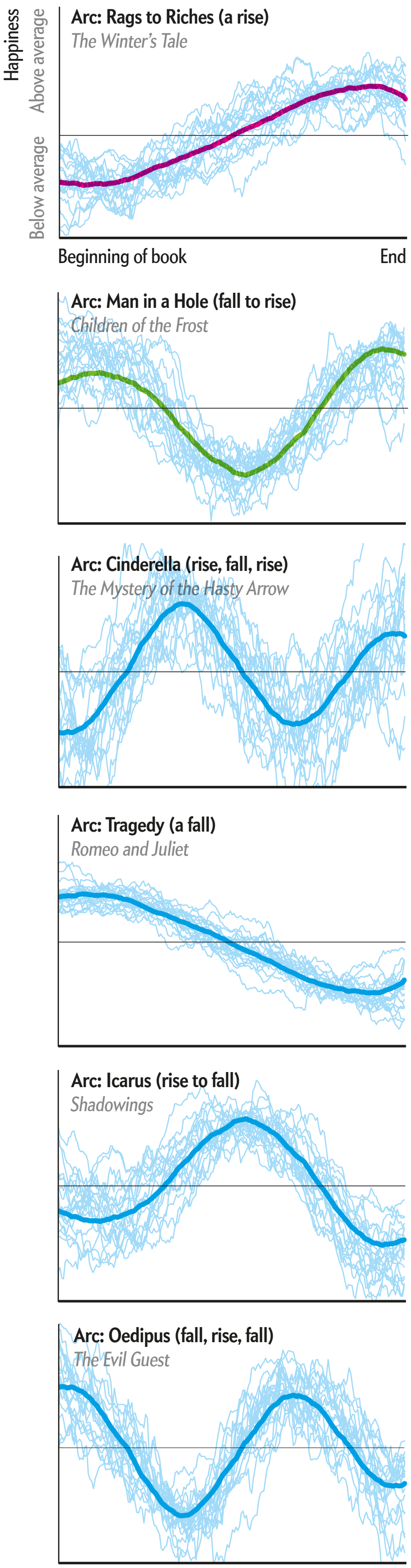
Great literature is surprisingly arithmetic

A good book evokes a variety of emotions as you read. Turns out, though, that almost all novels and plays provide one of only six "emotional experiences" from beginning to end—a rags-to-riches exuberance, say, or a rise and fall of hope (*left*). Researchers at the University of Vermont graphed the happiness and sadness of words that occurred across the pages of more than 1,300 fiction works to reveal the emotional arcs and discovered relatively few variations.

A different study coordinated by Poland's Institute of Nuclear Physics found that sentence lengths in books frequently form a fractal pattern—a set of objects that repeat on a small and large scale, the way small, triangular leaflets make up larger, triangular leaves that make up a larger, triangular palm frond (*below*).

Why analyze the mathematics of literature? Vermont applied mathematician Andrew J. Reagan notes that "tons of data" from the Human Genome Project "taught us so much more about genes than we knew before. Maybe data can teach us more about stories, too."

—*Mark Fischetti*

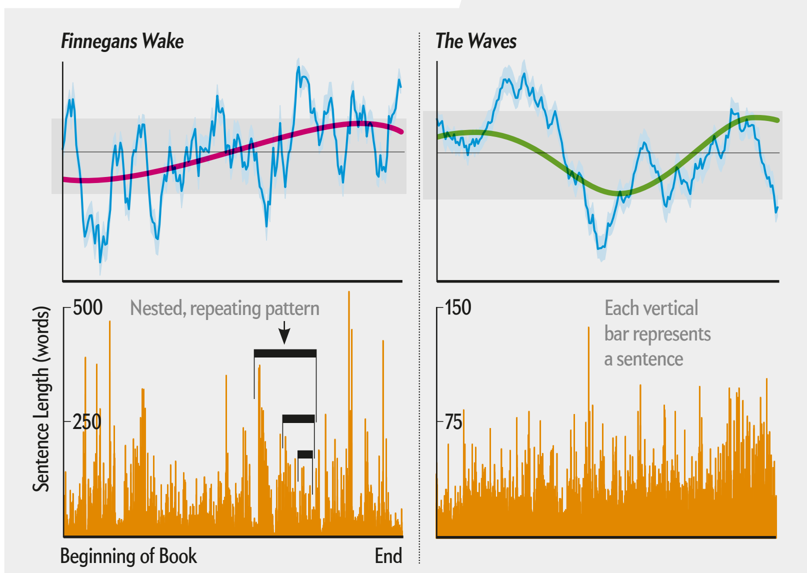


Emotional Arcs

About 85 percent of 1,327 fiction stories in the digitized Project Gutenberg collection follow one of six emotional arcs—a pattern of highs and lows from beginning to end (*dark curves*). The arcs are defined by the happiness or sadness of words in the running text (*jagged plots*). All books were in English and less than 100,000 words; examples are noted.

Crossover

At *Scientific American*'s request, Vermont researchers analyzed two books from a sentence fractal study (*bottom*) and found that the books did fit two of the common emotional arcs (*colored curves*). Do books that have the same kind of arc tend to have similar fractal patterns, too? No one knows yet.



Fractal Sentence Structure

The order and length of sentences in 113 famous literary works written in different languages almost always form fractal patterns. Stream of consciousness books such as *Finnegans Wake*, by James Joyce, had extreme repetitions. More traditional books such as *The Waves*, by Virginia Woolf, had more moderate repetitions. Both kinds were fractal.

SOURCES: "THE EMOTIONAL ARCS OF STORIES ARE DOMINATED BY SIX BASIC SHAPES," BY ANDREW J. REAGAN ET AL., IN *EPJ DATA SCIENCE*, VOL. 5, NO. 1, ARTICLE NO. 31; DECEMBER 2016 (*arcs*); "QUANTIFYING ORIGIN AND CHARACTER OF LONG-RANGE CORRELATIONS IN NARRATIVE TEXTS," BY STANISŁAW DROŻDŻ ET AL., IN *INFORMATION SCIENCES*, VOL. 331; FEBRUARY 20, 2016 (*fractals*)

Graphics by Andrew J. Reagan (emotional arcs) and Jen Christiansen (fractal charts)