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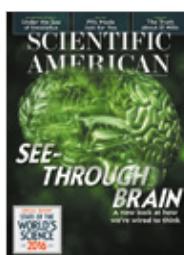
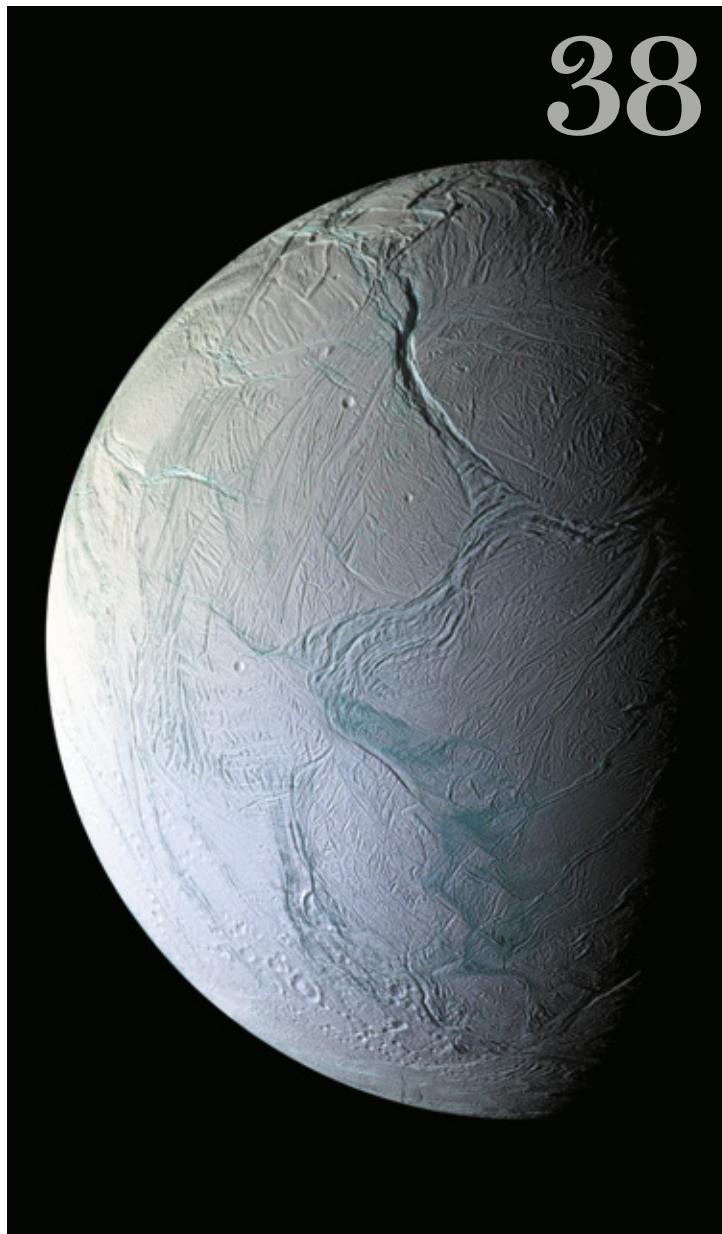
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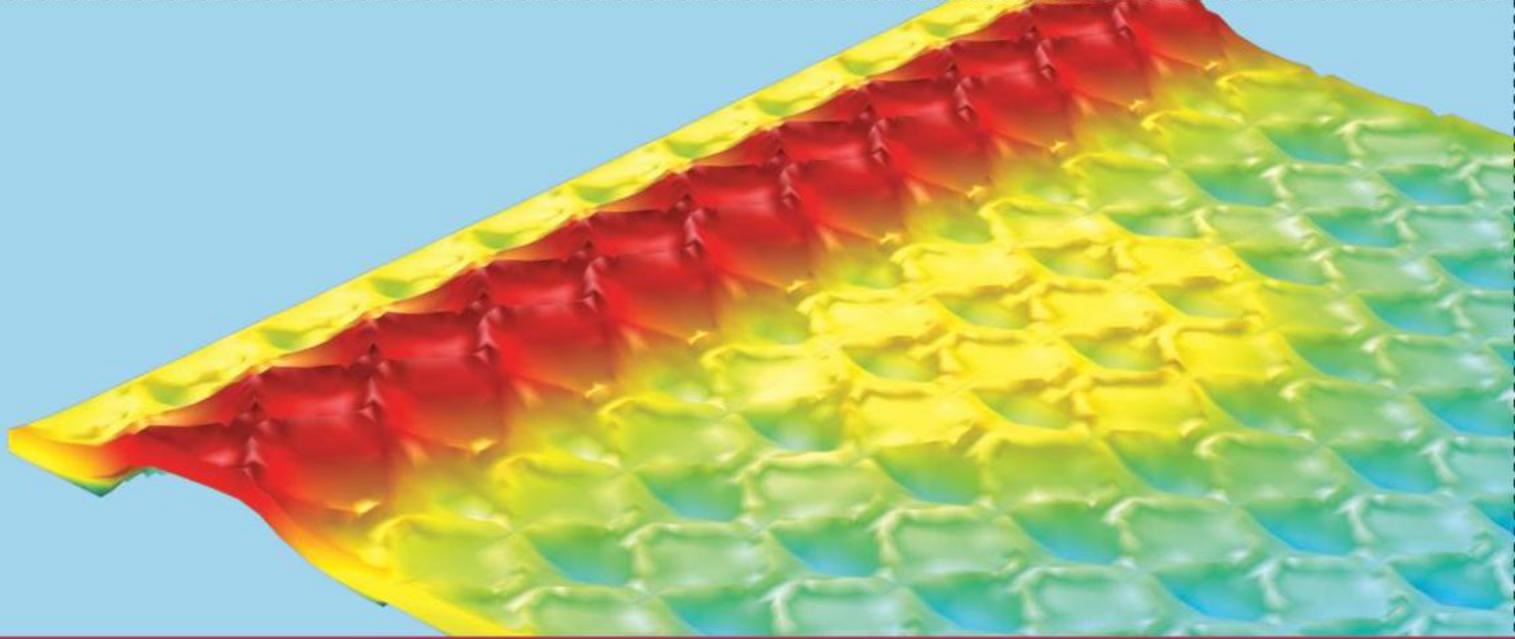
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New technologies for removing fats from the brain allow scientists to peer inside, revealing complex structures that process sensory information, store memories and help us make decisions about what to do next. Illustration by Maciej Frólow.



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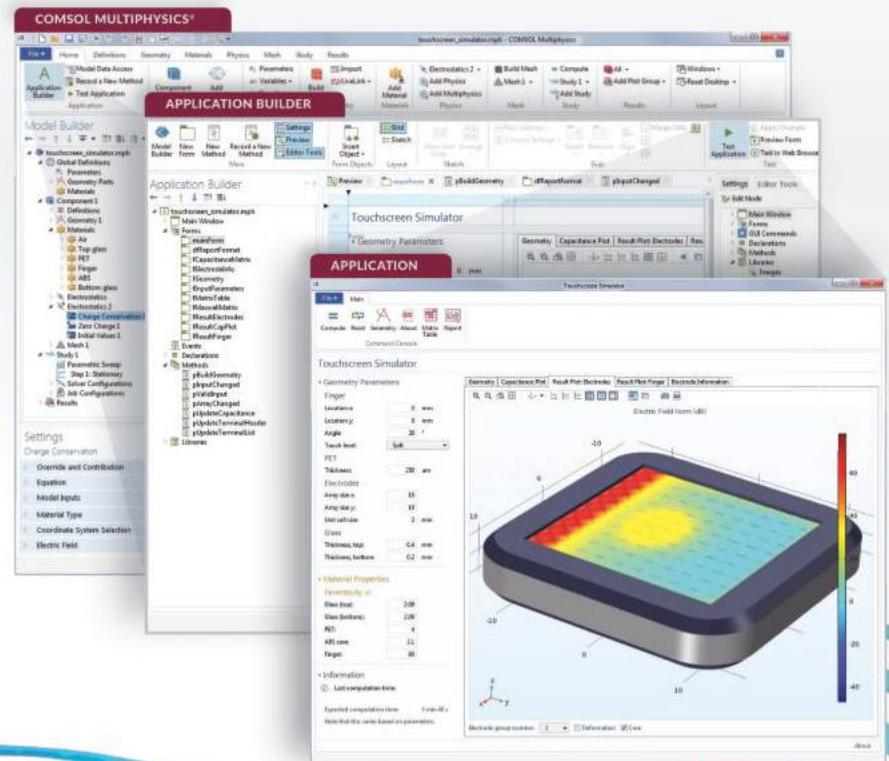
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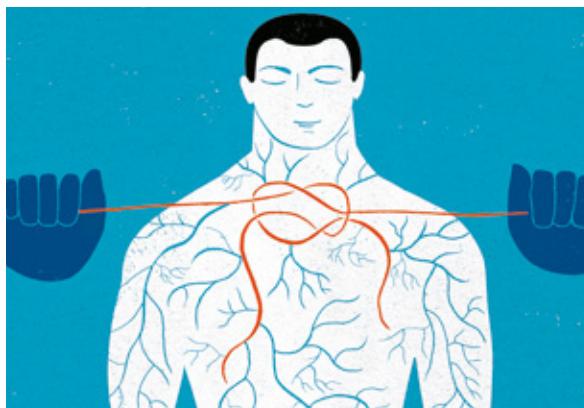
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Go to www.ScientificAmerican.com/oct2016/yellow-fever

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

New Views: Brains, Sciences, Oceans

We often casually say that we are “hardwired” to feel certain ways or to have specific responses to events. But what do we really know about that neural wiring? How does it wend through the gelatinlike brain that contains all our hopes and dreams, all that makes us who we are?

First of all, the telecom analogy isn’t that far off. Our nervous system uses the fibers known as axons to ferry information, in the form of electrical signals, among nerve cells. How, however, can scientists observe what bioengineer and psychiatrist Karl Deisseroth calls this “neuronal tapestry” when the tissue around it is decidedly opaque?

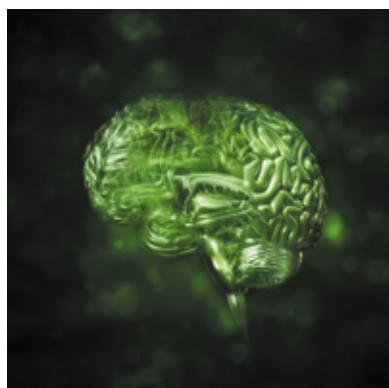
Our cover story, by Deisseroth, beginning on page 30, examines an exciting new technology that provides “A Look inside the Brain.” Scientists use polymers called hydrogels to create a see-through organ that retains its neural structures. This area of research has already begun to yield insights that will help us understand disorders such as parkinsonism, Alzhei-

mer’s disease, multiple sclerosis and autism, among others. In addition to detailing the findings, the article also does something else that is uniquely characteristic of *Scientific American*: it narrates a personal scientific journey of discovery, told by the investigator himself, with rich informational explanatory graphics, for which our art team is widely admired.

I do admit to a bit of a lifelong obsession about sharing the stories of science, especially given its role as a key driver of human progress. It’s part of why I wanted us to create the annual “State of the World’s Science,” which we began a few years ago—a vision that executive editor Fred Guterl has made into a reality. In this year’s report, we look at the challenges of communication for science: when that knowledge sharing is limited by others and when limiting occurs within the research communities themselves.

See page 52 for the start of the section.

Is there anyone in our audience who doesn’t enjoy a scientific mystery? What, for instance, lies “Under the Sea of Enceladus”? This article, by Frank Postberg, Ga-



briel Tobie and Thorsten Dambeck (page 38), describes the increasing evidence for hydrothermal vents in the depths of one of Saturn’s moons. On Earth, such bubbling vents are alive with fantastic-looking creatures, producing clusters of activity on an ocean bottom that can be otherwise forbidding. Could these vents be a place to look for life beyond our world? Another bit of intrigue for our marvelously wired brain networks to explore. ■

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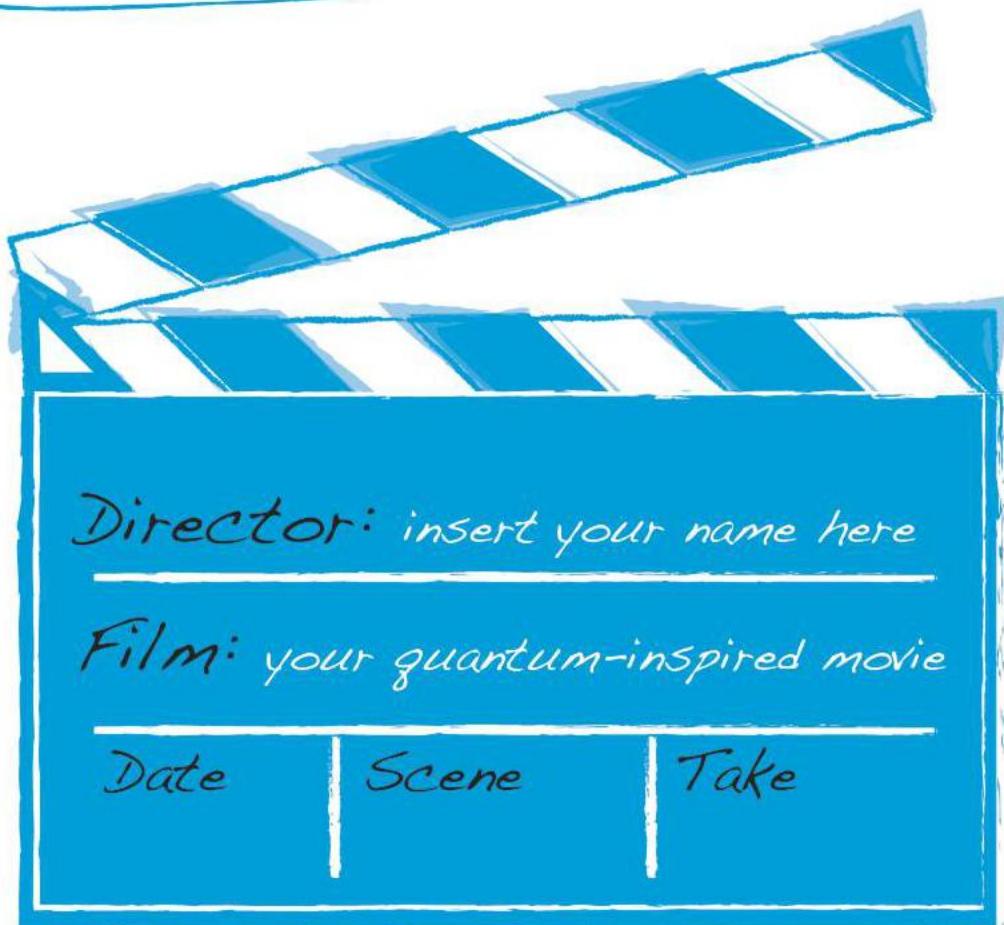
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LETTERS

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June 2016

SELF-DRIVING CARS

In "The Truth about 'Self-Driving' Cars," Steven E. Shladover strikes a welcome note of sanity in the hype about the predicted advent of automated vehicles on our roads. Yet when he describes "bus-and truck-platoon systems" as among the kind of automated vehicles we are likely to see sooner, it brought instantly to mind systems that have long been in place and that we are all familiar with: namely, freight and passenger trains.

The railway infrastructure has, of course, suffered long-term neglect, but the interstate highway network itself is not without its problems and would require an upgrade of serious proportions to meet the requirements of such systems.

MICHAEL J. REYNOLDS
Somerset, England

Self-driving cars just have to be better than humans, not perfect. There are plenty of YouTube videos showing the problems that humans have with snow and ice, and San Francisco attests to the fact that humans have a hard time driving in an urban environment. Also, we let seniors drive even when we know they will sometimes experience delayed responses.

CHUCK SIMMONS
Redwood City, Calif.

There are two areas the author did not mention that also affect the likelihood of

"Self-driving cars just have to be better than humans, not perfect."

CHUCK SIMMONS *REDWOOD CITY, CALIF.*

success. First, vehicles are typically privately owned and maintained, and their complex systems may not be properly cared for or updated. Second, public highways are also not always well maintained, especially in terms of traffic controls that disappear in inclement conditions.

But the potential benefits are immense, and on freeways, automated cars could reliably travel much closer together at highway speeds, providing for two to three times the traffic in existing lanes relatively congestion-free.

GARY KRUGER
Portland, Ore.

SMART FISH

In "Einstein of the Sea," Jonathan Balcombe describes behaviors exhibited by fish that involve the use of external objects in accomplishing certain tasks as "tool use." Even if the fishes' behavior is undeniably remarkable, the word "tool" can be deeply misleading. Human tool use involves mental images of the starting conditions and desired result and a plan leading from the one to the other. The use of "tools" by animals should not be mistaken for these abilities.

WILLIAM L. ABLER
Arcata, Calif.

BALCOMBE REPLIES: *Tool use by fishes might not differ from our own tool use as much as Abler believes. Fishes' capacity to communicate with referential signals and to execute sequential tasks in a flexible manner strongly supports their ability to plan, and their ability to remember and to create mental maps invokes a form of mental image making.*

GUNS AND SUICIDE

"A Plan to Prevent Gun Suicides" [The Science of Health], Nancy Shute's report about a "public safety campaign ... consisting mainly of distributing posters and brochures about suicide to gun

shops," is nothing but a feel-good piece.

Among recommendations from the advocacy organization Ceasefire Oregon is a period of delay between purchase of a gun and delivery of the gun to a customer to frustrate those who come to a gun shop with homicide or suicide in mind. What do you think the gun shop owners that Shute portrays as saintly would think of that?

CHARLIE McKEON
via e-mail

I lost my dear brother-in-law to suicide. He purchased a gun and four months later used it to take his own life.

I'm wondering if part of buying a gun could include two items: a case that has motivational quotes and the suicide prevention hotline on the outside and inside and a newsletter on how to ask for help and stories of people who have overcome the toughest of situations.

KATHRYN WILLIAMS
via e-mail

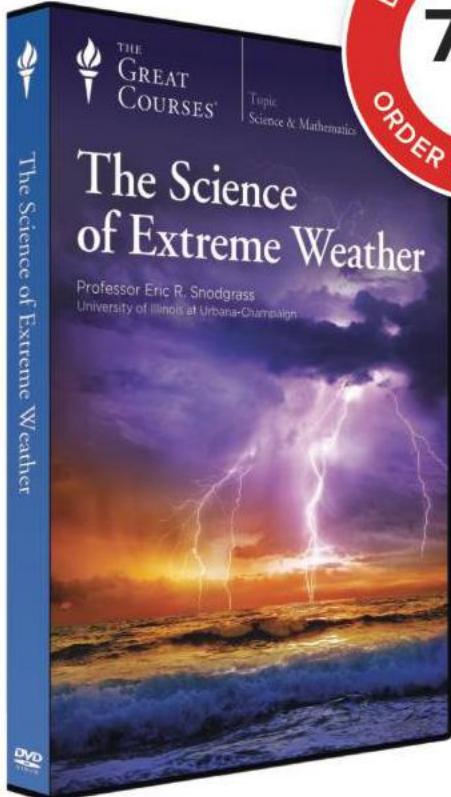
BRAIN VS. BITS

I find the capacities of the artificial neural networks described by Yoshua Bengio in "Machines Who Learn" far from brainy. The human brain can manage simple pattern analysis that is far beyond present AI abilities: The June issue of *Scientific American* lies upside down in front of me. Stacked side by side on the break-front are 18 books. Half the books and the June issue display the word "the" in their titles. The "the"s vary in font, style and position, and the *SA* cover is inverted. My coordinated eyes and brain have no difficulty comprehending "the" in all these formats. From the article's description of current AI sophistication, neural networks have a long way to go before they can begin to approximate human capacities for this simple word identification.

DAVID WERDEGAR
Naperville, Ill.

THOUGHTS ON DEATH ROW

Michael Shermer investigates the causes of death-row inmates' displays of positivity in "Death Wish" [Skeptic]. Although I am not on death row, I have served five years of a life sentence, so I may have some insight into this. As a felon, you come to grips with the fact that most of society



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LETTERS

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would rather be done with you. Couple that with a dangerous environment that often appears to an inmate to be as humiliating and demoralizing as possible, and, well, death becomes a less terrifying proposition. In short, what do you have to lose? Once you acknowledge that situation, it seems natural to focus on those bright points in your past and reinforce them instead of the monotony of your present life.

GORDON SCHUMACHER
Canon City, Colo.

SHERMER REPLIES: The problem that Schumacher identifies in the prison system is largely the result of the U.S. still mainly engaging in "retributive justice," or the understandable desire for revenge and to give criminals their "just desserts," instead of "restorative justice," or the attempt to repair the damage done to the victim and to rehabilitate the perpetrator. Many countries are experimenting with complementing retribution with restoration, to great effect for victims, perpetrators and society.

CLARIFICATIONS

"The Fog of Agent Orange," by Charles Schmidt, referred to the U.S. Department of Veterans Affairs as offering compensation to Vietnam War veterans and their children for particular illnesses that have been linked to exposure to Agent Orange if exposure had been proved. It should have noted that the department considers a veteran's presence in Vietnam or the Korean demilitarized zone during specified periods between 1962 and 1975 to be sufficient evidence of exposure.

In the August 2016 issue the box "Bill Gates on Global Health" in "Health Check for Humanity," by W. Wayt Gibbs, should have stated that the interview with Gates was conducted in April 2014.

ERRATA

"The Collider That Could Save Physics," by Howard Baer, Vernon D. Barger and Jenny List [Forum], incorrectly gives the energy released by matter-antimatter annihilations in the proposed International Linear Collider as 250 billion electron volts. It would be 500 billion. Further, the article should have referred to the Large Hadron Collider as producing proton-proton collisions, not proton-antiproton.

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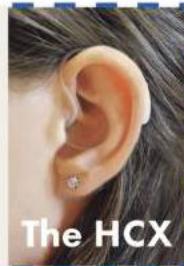


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Science Is Not Enough

Politicians trying to dump humanities education will hobble our economy

By the Editors

Kentucky governor Matt Bevin wants students majoring in electrical engineering to receive state subsidies for their education but doesn't want to support those who study subjects such as French literature. Bevin is not alone in trying to nudge higher education toward course work that promotes better future job prospects. Senator Marco Rubio of Florida, a former presidential candidate, put it bluntly last year by calling for more welders and fewer philosophers.

Promoting science and technology education to the exclusion of the humanities may seem like a good idea, but it is deeply misguided. *Scientific American* has always been an ardent supporter of teaching STEM: science, technology, engineering and mathematics. But studying the interaction of genes or engaging in a graduate-level project to develop software for self-driving cars should not edge out majoring in the classics or art history.

The need to teach both music theory and string theory is a necessity for the U.S. economy to continue as the preeminent leader in technological innovation. The unparalleled dynamism of Silicon Valley and Hollywood requires intimate ties that unite what scientist and novelist C. P. Snow called the “two cultures” of the arts and sciences.

Steve Jobs, who reigned for decades as a tech hero, was neither a coder nor a hardware engineer. He stood out among the tech elite because he brought an artistic sensibility to the redesign of clunky mobile phones and desktop computers. Jobs once declared: “It’s in Apple’s DNA that technology alone is not enough—that it’s technology married with liberal arts, married with the humanities, that yields us the result that makes our hearts sing.”

A seeming link between innovation and the liberal arts now intrigues countries where broad-based education is less prevalent. In most of the world, university curricula still emphasize learning skills oriented toward a specific profession or trade. The ebullience of the U.S. economy, which boasted in 2014 the highest percentage of high-tech outfits among all its public companies—has spurred countries such as Singapore to create schools fashioned after the U.S. liberal arts model.

If Bevin and other advocates of a STEM-only curriculum look more closely, they will find that the student who graduates after four years of pursuing physics *plus* poetry may, in fact, be just the kind of job candidate sought out by employers. In 2013 the Association of American Colleges & Universities issued the results of a survey of 318 employers with 25 or more employees showing that nearly all of them thought that the ability to



“think critically, communicate clearly, and solve complex problems”—the precise objectives of any liberal arts education—was more important than a job candidate’s specific major.

Those same skills, moreover, are precisely the ones required for marrying artistic design with the engineering refinements needed to differentiate high-end cars, clothes or cell phones from legions of marketplace competitors—the type of expertise, in fact, that is least likely to be threatened by computers, robots and other job usurpers. “Consider America’s vast entertainment industry, built around stories, songs, design and creativity,” wrote commentator Fareed Zakaria, author of the book *In Defense of a Liberal Education*, in a *Washington Post* column. “All of this requires skills far beyond the offerings of a narrow STEM curriculum.”

The undergraduate able to cobble together a course schedule integrating STEM and the humanities may be able to reap rich rewards. Facebook co-founder Mark Zuckerberg became an avid student of Greek and Latin when he was only in high school, in addition to setting about learning programming languages. And the same government officials who call for a shift in educational priorities should know better than to trash the liberal arts. Take Bevin’s call to eschew French literature: Bevin is someone with his own debt to the humanities. He graduated from college with a bachelor’s degree in East Asian studies.

The way to encourage high-tech industry to move to Kentucky—or any other state—is not to disparage Voltaire and Camus. Rather the goal should be to build a topflight state educational system and ease the way financially for students from even the most humble backgrounds to attend. The jobs will follow—whether they be in state government or in social media start-ups. ■

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Carl Hart is a professor of psychology at Columbia University. He is also author of the book *High Price: A Neuroscientist's Journey of Self-Discovery That Challenges Everything You Know about Drugs and Society*, winner of the 2014 PEN/E. O. Wilson Literary Science Writing Award.

Our Senseless Pot Laws

Keeping existing federal rules in place is an exercise in hypocrisy

By Carl Hart

In early August the Drug Enforcement Administration declined to reclassify marijuana under the federal Controlled Substances Act. The drug is currently listed on Schedule I, meaning that it is viewed as having “no currently accepted medical use in treatment” and is therefore technically banned by federal law. The proposed change would have moved it to Schedule II, where it would join morphine, opium and codeine. That would make marijuana potentially available by prescription nationwide. Such a change would have been good for patients and scientists, and it would have represented a big step toward resolving the hypocritical mess that characterizes current law.

Despite many people’s assumptions to the contrary, the existing law does not ban scientific investigation into the harms and benefits of the drug. It’s true that scientists studying marijuana must jump through multiple bureaucratic and regulatory hoops, and one of these just became a bit easier to navigate.

Currently researchers who want to study the drug must get it from the University of Mississippi, which is the only university now permitted to grow marijuana plants for research purposes. When the DEA announced in August that it would not reschedule marijuana, it *did* say that it would let other institutions apply for permission to start growing the plants as well. That was a step in the right direction—but it’s not enough.

Despite the regulatory barriers, dozens of scientists—myself included—have been engaged in research on the harms and benefits of marijuana for decades, and the evidence shows that the drug has many helpful therapeutic uses. For example, it stimulates appetite in HIV-positive patients, which could be a lifesaver for someone suffering from AIDS wasting syndrome. It is also useful in the treatment of neuropathic pain, chronic pain, and spasticity caused by multiple sclerosis.

Therapeutic benefits such as these have compelled citizens to vote repeatedly, over the past two decades, to legalize medical marijuana at the state level. Today 25 states and the District of Columbia allow patients to take the drug for specific conditions. And yet federal law still technically forbids the use of medical marijuana. The inconsistency of federal law with reality at the state level—and with the growing body of research demonstrating the benefits of the substance—makes marijuana’s Schedule I status seem like medical and bureaucratic hypocrisy.

There is now a general sentiment among scientists that the



failed war on drugs has biased the DEA against acknowledging *any* therapeutic potential for marijuana. The petition to reschedule the substance that the agency responded to this past summer was *five years old*. It is hard to avoid the impression that DEA leadership was stalling, hoping that the public would simply forget about the issue. Last year DEA acting administrator Chuck Rosenberg described the very concept of medical marijuana as “a joke.”

Perhaps it’s also a joke that a law-enforcement agency has the final word on a medical issue.

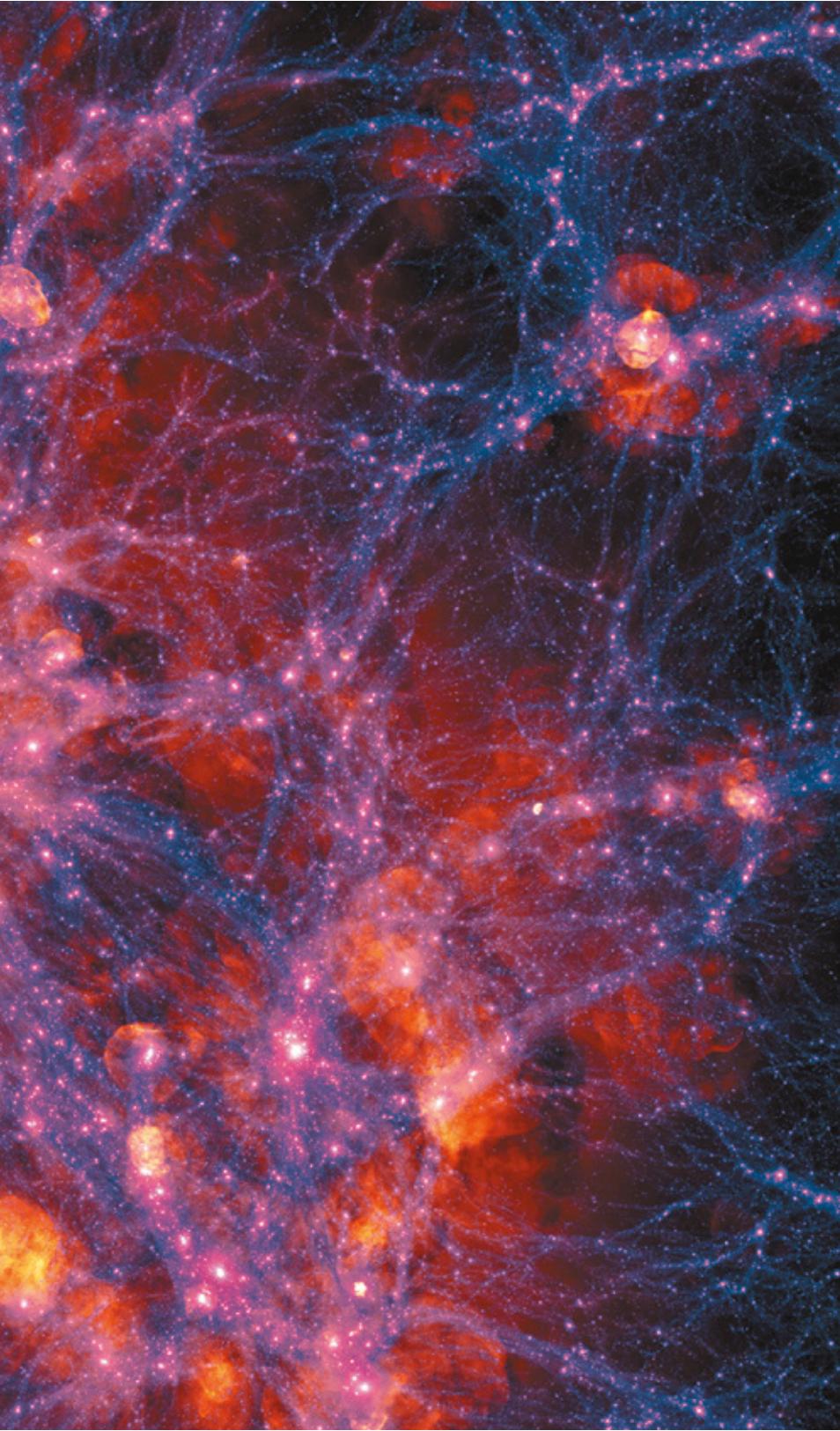
As a scientist and educator, I am worried that our illogical, unscientific scheduling of marijuana is costing us credibility with young people and with those seeking treatments for a variety of conditions. I am further concerned that people most in need of our help and advice will reject other drug-related information from “official” sources, even when it is accurate. And when patients reject official advice and proved medicine, they become more susceptible to quackery. It’s time we lessened the outsized influence of a law-enforcement agency on medical decisions and started to rebuild our credibility as scientists on the issue of marijuana. ■

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ADVANCES



- Two decades after cloning, how have the Dollys fared?
- The National Weather Service gets next-generation satellites
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- An Arctic archaeologist races against melting ice



PHYSICS

In the Dark about Dark Matter

Recent disappointments have physicists looking beyond WIMPs for dark matter particles

Physics has missed a long-scheduled appointment with its future—again. The latest, most sensitive searches for the particles thought to make up dark matter—the invisible stuff that may compose 85 percent of the mass in the cosmos—have found nothing. These elusive particles, called WIMPs (weakly interacting massive particles), may simply be better at hiding than physicists thought. Alternatively, they may not exist, which would mean that something is woefully amiss in the underpinnings of how we try to make sense of the universe. Many scientists still hold out hope that upgraded versions of the experiments looking for WIMPs will find them, but others are taking a second look at conceptions of dark matter long deemed unlikely.

The first null result this summer came from the Large Underground Xenon (LUX) experiment, a third of a metric ton of liquid xenon held at a frosty -100 degrees Celsius inside a giant, water-filled tank buried one and a half kilometers under the Black Hills of South Dakota. There, shielded from most sources of contaminating radiation, researchers have spent more than a year's worth of time looking for flashes of light emanating from WIMPs striking xenon nuclei. On

July 21 they announced they had seen none.

The second disappointing report came on August 5 from the most powerful particle accelerator ever built: CERN's Large Hadron Collider (LHC) near Geneva. Since the spring of 2015, the LHC has been pursuing WIMPs by smashing protons together at unprecedentedly high energies, at rates of up to a billion collisions per second, pushing into new frontiers of particle physics. Early on, two teams had spied a telltale anomaly in the subatomic wreckage: an excess of energy from proton collisions that hinted at new physics perhaps produced by WIMPs (or, to be fair, many additional exotic possibilities). Instead, as the LHC smashed more protons and collected more data, the anomaly fizzled out, indicating it had been a statistical fluke.

Taken together, these two null results are a double-edged sword for dark matter. On one hand, their new constraints on the plausible masses and interactions of WIMPs are priming plans for next-generation detectors that could offer better chances of success. On the other, they have ruled out some of the simplest and most cherished WIMP models, raising fresh fears that WIMPs might be a multidecadal detour in the search for dark matter.

Edward "Rocky" Kolb, a cosmologist now at the University of Chicago who in the 1970s helped to lay the foundation for WIMP hunts, has declared the 2010s "the Decade of the WIMP" but now admits the search hasn't gone as planned. "We are now more in the dark about dark matter than we were five years ago," he says. So far, Kolb notes, most theorists have responded by "letting a thousand WIMPs bloom," creating ever more baroque and exotic theories to explain how the supposedly ubiquitous particles have dodged all our detectors.

Theorists have two intertwined reasons to hunt for WIMPs. The first is that WIMPs are a natural consequence of the most popular extensions to the Standard Model of particle physics, which predicts their production shortly after the big bang. The second is that if such primordial WIMPs exist, straightforward calculations suggest their present-day abundance and behavior should now almost exactly match the quantities and qualities of dark matter inferred from observations. This so-called WIMP miracle has sustained the search for decades, but now some theorists are questioning its validity.

For example, in 2008 Jonathan Feng and Jason Kumar, both then at the University of California, Irvine, showed how a phenomenon known as supersymmetry could produce a hypothetical class of particles much lighter and more weakly interacting than WIMPs. "These particles result in the same amount of dark matter we see today, but they aren't WIMPs," Feng says. "This upsets the apple cart because it is just as well motivated theoretically. We call it the WIMPless miracle."

The decaying theoretical underpinnings for simple WIMP models, paired with

"These particles result in the same amount of dark matter we see today, but they aren't WIMPs."
—Jonathan Feng
U.C. Irvine

the growing list of empty-handed detection efforts, have led Feng and many others to propose that WIMPs are part of a more complicated picture: a hidden realm of the universe filled with varieties of dark particles interacting with one another through a suite of dark forces, perhaps exchanging dark charges through bursts of dark light. Because they offer theorists many more variables to play with, such "dark sector" models can be reconciled to fit into the ever tighter straitjacket of facts placed on dark matter by new data—but the downside is that this sprawling flexibility makes them very difficult to conclusively test.

"With the dark sector, you're free to invent almost whatever you want," says David Spergel, an astrophysicist at Princeton University. "Now that we have lost the guidance from the WIMP miracle, the space of available models is huge. It's a playground where we don't know what the right choices are—we now need more hints from nature about where to go next."

Some physicists, following nature's hints, have abandoned WIMPs altogeth-

er. For instance, ghostly particles called neutrinos are known to exist and come in three varieties, or flavors. Although the three varieties are not massive enough to account for dark matter, by virtue of having mass at all they open the possibility for the existence of a fourth—a massive, so-called sterile neutrino. "Almost all neutrino mass-generation mechanisms require the existence of sterile neutrinos, and it would be very easy for some of these sterile neutrinos to account for the dark matter," says Kevork Abazajian, a theorist at U.C. Irvine.

Another perennial dark horse candidate for dark matter is the axion, a hypothetical weakly interacting particle first postulated in 1977 to explain and resolve otherwise mysterious asymmetries in quantum interactions. For axions to explain dark matter, they would need to occupy a relatively narrow range of masses and be far lighter than WIMPs. "If we don't find the WIMP, theorists will just switch their bets to axions," says Peter Graham, a physicist at Stanford University.

Beyond WIMPs and dark sectors, sterile neutrinos and axions, there are even more exotic possibilities for dark matter, although they occupy the fringes of physics, including "primordial" black holes, extra dimensions and the possibility that Einstein's theory of gravity is wrong in some way.

Whatever their preferred candidate might be, the biggest concern for many physicists grappling with dark matter is not that the concept will eventually be seen as somehow invalid or entirely mistaken—the observational evidence for dark matter's existence is overwhelming. Instead they worry that dark matter's identity might simply prove to be irrelevant to other great mysteries in physics and thus offer no new paths toward understanding the true nature of reality.

"The desire is for dark matter not only to exist but also to solve other outstanding problems of the Standard Model," says Jesse Thaler, a physicist at the Massachusetts Institute of Technology. "Not every new discovery can be a revelation ... where afterward theories suddenly fit together much better. Sometimes new particles just make you say, 'Who ordered that?' Do we live in a universe where each discovery leads to deeper, more fundamental insights, or do we live in one where some parts have rhyme and reason, but others don't? Dark matter offers either possibility."

—Lee Billings

**GENETICS**

Send in the Clones

The first rigorous study of aging cloned animals reveals they are perfectly normal

The birth of Dolly the sheep 20 years ago proved that DNA from an adult cell of a mammal could be transferred to an unfertilized egg and give rise to an animal genetically identical to the donor. Yet Dolly died prematurely, which left the impression that cloned animals have shorter life spans.

To figure out if clones are inherently less healthy than their “natural” counterparts, University of Nottingham developmental biologist Kevin Sinclair followed four of Dolly’s clones—Debbie, Denise, Dianna and Daisy (above)—from birth through middle age. All four were derived from the same batch of frozen mammary gland cells as Dolly was. Sinclair and his colleagues also monitored nine cloned sheep of other breeds. The 13 ruminants are now more than nine years old—the equivalent of a human’s seventh or eighth decade—and all are as healthy as regular sheep, according to scans of their bones, blood glucose readings and detailed blood pressure monitoring. “We can say these [clones] are perfectly normal,” Sinclair says. The results were published in *Nature Communications*.

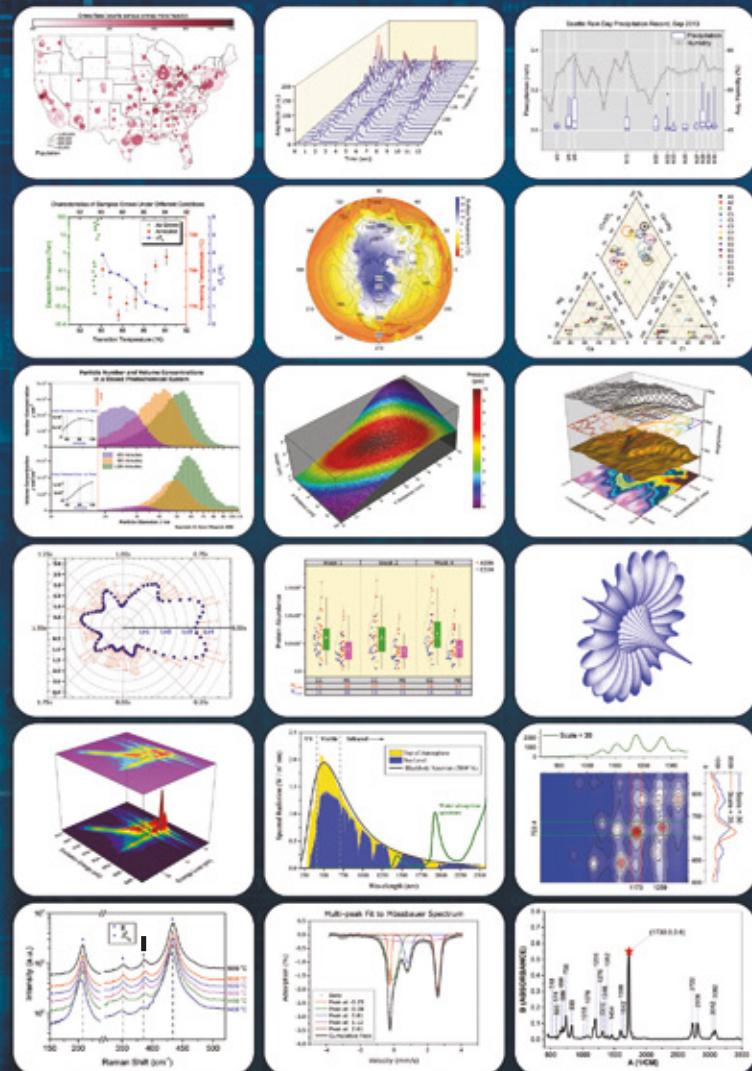
So why did Dolly die young? The scientists who worked with her say she died from a contagious illness that spread through the flock—not because of any problem specific to clones. She did have some arthritis in her knees, but geneticist Helen Sang of the Roslin Institute in Edinburgh, where Dolly was born, notes that any sheep kept inside and fed treats as often as Dolly was would be subject to joint problems.

Two decades later cloning is still less efficient than normal breeding. But the new study shows that if a cloned animal survives gestation and is in good health during the first few weeks of life, it is likely to have the same chances of thriving as other animals of its breed. Cloning is used today to generate embryonic stem cells for research and to breed high-value livestock. Long live the copies!

—Karen Weintraub

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METEOROLOGY

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The next generation of U.S. weather satellites includes lightning detection and near-constant monitoring of severe storms

Daily weather forecasts in the U.S. wouldn't be nearly as accurate as they are without the three geostationary weather satellites that are parked 22,000 miles above Earth. Next month these predictions will get even better: the U.S. National Oceanic and Atmospheric Administration and NASA plan to launch the first of four satellites that should deliver what the agencies call "game-changing" capabilities for predicting both ordinary weather and dangerous storms such as hurricanes. These next-generation spacecraft are needed to replace the existing weather satellites, one of which reaches the end of its operational lifetime this year.



The new Geostationary Operational Environmental Satellite-R (GOES-R) will have the ability to scan for signs of rain, snow and lightning in the clouds above the entire continental U.S. every five minutes and to take smaller, focused images of problem areas every 30 seconds. By comparison, the older versions of GOES take images of the continental U.S. every 30 minutes and cannot simultaneously capture focused images. "The ability to observe regions every 30 seconds will allow forecasters to see what is happening in near real time and provide information not captured

in current satellite imagery, such as the formation and evolution of rapidly developing severe weather," says Greg Mandt, system program manager for GOES-R at NOAA. "This will enable more advanced warnings and effective evacuations."

Satellite imagery contributes heavily to the National Weather Service maps that show and predict the movement of storm clouds. GOES-R would collect three times more data, provide four times better image resolution and enable more than five times faster coverage in comparison with the older satellites.

The updated satellite will also feature an instrument that represents the first of its kind in orbit: a lightning mapper. This high-speed, near-infrared camera will detect lightning flashes over North and South America as well as the surrounding oceans, enabling forecasters to issue earlier warnings for severe storms. There are also onboard instruments to watch the sun and detect dangerous solar storms that can hurl charged electromagnetic particles at Earth. Better space weather forecasting could provide notifications of potential disruptions to power grids and satellite fleets.

Much is riding on the planned November 4 launch of the first GOES-R satellite. The initial launch, which was slated for last October, has already been delayed twice because of budget issues and launch schedule problems. But more delays could mean NOAA may not have a backup weather satellite ready in the event that an operational satellite malfunctions. Any potential gaps in weather coverage could prove costly. In 2015 alone there were 10 weather or climate disasters—each costing the U.S. more than \$1 billion in damage. "Investing in this satellite system is an investment in our safety," Mandt says.

—Jeremy Hsu

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Depressed? Do What You Love

Therapies that focus on changing behaviors are just as effective as those that modify thoughts in managing the debilitating mood disorder

About 350 million people around the world suffer from depression. Therapists can use many different techniques to help, but none has more rigorous scientific evidence behind it than cognitive-behavioral therapy (CBT). This “inside-out” technique focuses primarily on thought patterns, training patients to recognize and reframe problematic thinking. Now, however, mental health professionals have another option: mounting evidence shows that a technique called behavioral-activation (BA) therapy is just as effective as CBT.

BA is an outside-in technique in which therapists focus on modifying actions rather than thoughts. “The idea is that what you do and how you feel are linked,” says David Richards, a health services researcher at the University of Exeter in England. If a patient values nature and family, for example, a therapist might encourage him to schedule a daily walk in the park with his grandchildren. Doing so could increase the rewards of engaging more with the outside world, which can be a struggle for depressed people, and could create an alternative to more negative pastimes such as ruminating on loss. BA has existed for decades, and some of its elements are used in CBT, yet until now it had never been tested with the scale and rigor needed to assess its relative strength as a stand-alone approach.

In one of the largest studies of its kind, Richards led a collaboration of 18 researchers working at three mental health centers in the U.K. who put BA and CBT head-to-head. They assigned 440 people with depression to about 16 weeks of one of the two approaches,



then followed the patients’ progress at six, 12 and 18 months after treatment began. As revealed in a paper, published online in July in the *Lancet*, the team found the treatments to be equally effective. A year on, about two thirds of the patients in both groups reported at least a 50 percent reduction in their symptoms.

These findings could change therapeutic

guidelines. For instance, patients with depression could begin with simpler therapies such as BA, then seek out more specialized care if they do not respond to that treatment. The approach is similar to the prescription of antidepressant medications, which have a success rate comparable to that of these therapies. “We believe that behavioral activation is a good first step in treatment, and this article addresses that point,” says Weill Cornell Medical College geriatric psychiatrist George Alexopoulos, who was not involved in the study.

In addition, Richards and his colleagues found that junior health workers could provide BA after a brief training period—making it significantly cheaper to implement than CBT, which requires highly specialized therapists. That distinction could make the former a boon to developing countries, where resources for mental health are especially scarce.

—Daisy Yuhas

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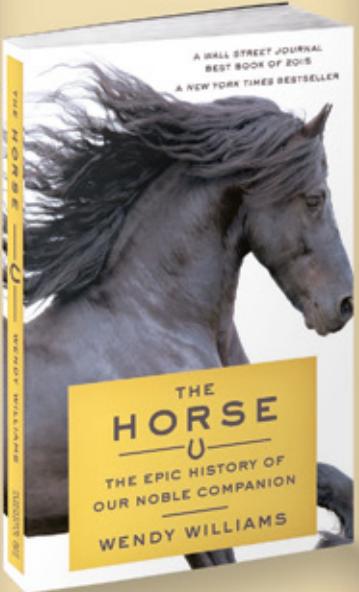
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ADVANCES

TECHNOLOGY

A Boost from Above

Babies at risk for cerebral palsy learn to crawl sooner and farther with a robot helper than they would on their own

For infants with cerebral palsy, crawling can be a challenge. The children, who suffer from brain damage that impairs muscle control, frequently give up trying to master moving across the floor. In turn, the brain stops building and reinforcing connections involved in developing motor skills and the ability to orient oneself in space, leading to further problems with movement later in life, says Thubi Kolobe, a physical therapist and researcher at the University of Oklahoma. "If you don't use it, you lose it—that's the motto of the brain," she explains.

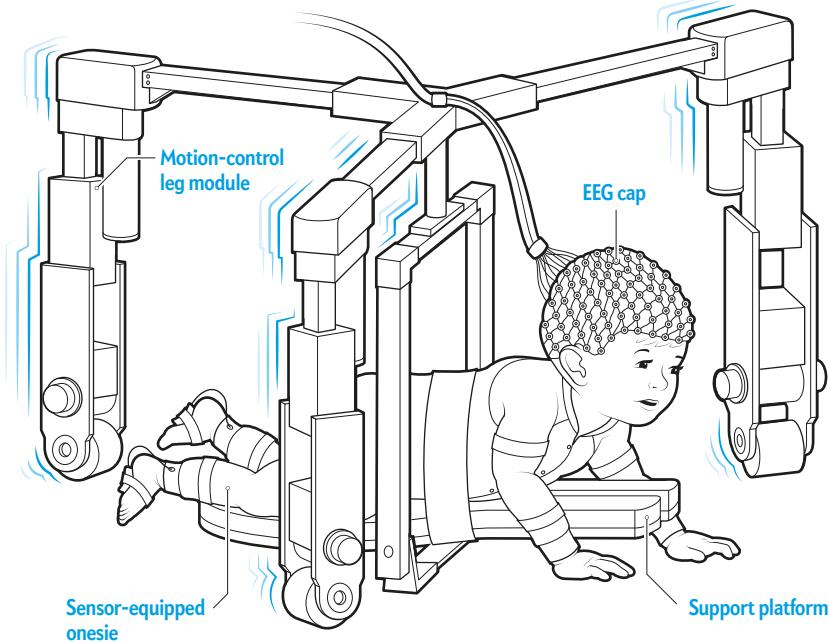
Following up on research showing that early intervention can improve motor control, Kolobe and her colleagues have developed a contraption meant to promote crawling. The device, called the Self-Initiated Prone Progression Crawler (SIPPC), consists of a high-tech onesie and a three-legged, wheeled robot equipped with a machine-learning algorithm. Sensors in the onesie detect a baby's kicks or shifts in weight, and the robot responds by pushing a support

platform in the same direction, giving the baby a boost toward where he or she wants to go. In a preliminary 12-week trial, the researchers observed 28 infants at risk for cerebral palsy as they practiced crawling twice a week with SIPPC (an official diagnosis for the disorder usually takes place after the age of one). Infants who received boosts from SIPPC were able to move around a room almost a month earlier than those in a group who practiced with an unpowered version of the robot. And when the researchers followed up at 14 months of age, they found that the movement-aided infants were more likely to crawl independently, too.

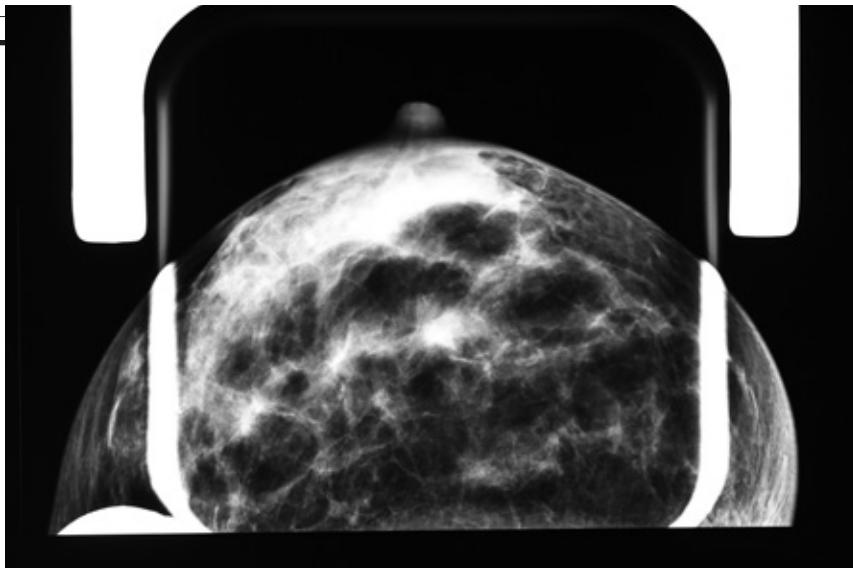
The team is now expanding the trial and plans to enroll nearly 80 infants at risk of cerebral palsy. "Our hope is that we'll ultimately be able to have a robot therapy that can give these children more motor experience and improve their ability to engage in society and be independent when they grow up," says bioengineering professor Andrew Fagg, a co-author of the study.

—Knvul Sheikh

The SIPPC robot supports infants in a crawling position as they learn how to explore their surroundings.



SOURCE: "NOVEL ASSISTIVE DEVICE FOR TEACHING CRAWLING SKILLS TO INFANTS," BY MUSTAFAA GHAZI ET AL., IN FIELD AND SERVICE ROBOTICS, EDITED BY DAVID S. WETTERGREEN AND TIMOTHY D. BARFOOT, SPRINGER INTERNATIONAL PUBLISHING, 2016



HEALTH

The Breast Has Its Own Microbiome

And the mix of bacteria could prevent or abet cancer growth

The gut microbiome has stolen the show when it comes to the recent explosion of research on the bacteria that thrive within us. But bacteria also live in a woman's breast tissue—and the mix of those microbes may have an equally important effect on health, according to a new study in *Applied and Environmental Microbiology*. The results "suggest that microbes in the breast, even in low amounts, may be playing a role in breast cancer—increasing the risk in some cases and decreasing the risk in other cases," says Gregor Reid, a professor of microbiology and immunology at Western University in Ontario and the study's senior author.

One in eight women in the U.S. are diagnosed with breast cancer during their lifetimes, but its origins remain unknown in most cases. Age, genetic predisposition and environmental changes are often implicated—and according to a growing body of research, bacteria may be one of those environmental factors. For instance, as early as the 1960s a number of studies have found that breast-feeding is associated with a lower risk of breast cancer, and more recent work suggests that this may be because breast milk supports the growth of beneficial microorganisms.

Reid and his team decided to pursue

this line of thought. They analyzed bacterial DNA found in breast tissue samples from 58 women who were undergoing lumpectomies or mastectomies for either benign or cancerous tumors, as well as from 23 healthy women who had undergone breast reductions or enhancements. They found that women with breast cancer had higher levels of some types of bacteria, including Enterobacteriaceae, *Staphylococcus* and *Bacillus*. Women without cancer had higher levels of other types, such as *Lactococcus* and *Streptococcus*.

It isn't surprising in and of itself that the breast harbors microbes, says immunologist Delphine Lee, who studies breast cancer at the John Wayne Cancer Institute in Santa Monica, Calif., and was not involved in the study. "The breast is exposed to the outside environment through the nipple and ductal system. Bacteria can also get in the tissue through skin wounds and other mechanisms," she explains. "But what we're not sure of yet is whether certain bacteria are found near breast tumors because they cause breast cancer or because they just thrive in the tumor environment."

If certain bacteria do instigate cancer, how would they do so? Some Enterobacteriaceae and *Staphylococcus* microbes seem to cause DNA damage—a known route to the development of cancer. Other bacteria may trigger inflammation. The exact mechanisms must be probed in further animal studies, Reid says, but eventually he hopes researchers will be able to use a patient's bacterial makeup as a biomarker for cancer screening or to develop probiotics for improving prognosis and treatment outcomes.

—Khnul Sheikh

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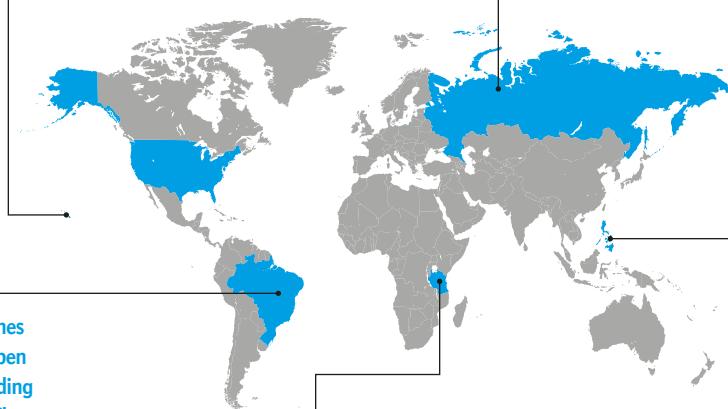
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IN THE NEWS

Quick Hits

U.S.

Pilots from more than 30 countries will converge on Hawaii this month to participate in the first annual World Drone Racing Championships.



RUSSIA

Anthrax hospitalized at least 90 people and killed one in northern Russia. Experts think the bacteria involved came from a reindeer carcass that had been frozen in the permafrost and melted after a streak of high temperatures. Scientists have warned of the spread of infectious diseases as the planet warms.

PHILIPPINES

The Philippines became the first country to make a dengue vaccine commercially available. The dengue fever virus infects 390 million people every year, mostly in Asia. Several Latin American countries are also now in various stages of rollout.

BRAZIL

Capuchin monkeys employed stones as hammers and anvils to crack open nuts at least 700 years ago, according to new archaeological evidence. The stones represent the oldest record of nonhuman tool use outside of Africa.

For more details, visit
www.ScientificAmerican.com/oct2016/advances

TANZANIA

Researchers discovered a natural reserve of helium in the Rift Valley—a finding that could help mitigate future shortages of the nonrenewable gas. Helium is used in MRI scanners, superconducting magnets and space exploration vehicles.

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ANIMAL BEHAVIOR

Taking Direction from a Deer

The startled mammals head due north or south to flee predators

When something frightens grazing deer, they all suddenly bound away together in an apparently organized fashion. How does a stressed-out, possibly panicked group of animals manage to coordinate such a getaway without crashing into one another?

In an effort to find out, biologist Hynek Burda of the Czech University of Life Sciences Prague and his team turned to roe deer, European ungulates that often graze in open

fields. As a favorite of hunters, the deer associate humans with danger and run away when approached. During the spring and summer of 2014 the researchers deliberately startled 188 groups of grazing deer in three different Czech hunting grounds.

It is reasonable to assume that the deer would run directly away from an approaching threat or toward the nearest cover. Instead the researchers discovered that the

animals preferred heading toward magnetic north or south.

To Burda, this observation suggests that roe deer might be able to detect the earth's magnetic field, as if they have an innate compass. "Magnetoreception is apparently a less exotic sense than usually assumed," he says. It may allow individuals in the herd to escape without colliding (because they head in the same direction), as well as to rapidly reassemble as a group once the threat has passed. The findings were published in August in *Behavioral Ecology and Sociobiology*.

Matthew Kauffman, a zoologist at the University of Wyoming who was not involved in the study, says the results are intriguing because researchers seldom consider geomagnetism as a strategy to avoid predators. But he adds that more evidence is needed to confirm the explanation and that Burda and his group should repeat the experiment in different places during different seasons. "Lots of things in the natural environment could correlate with the cardinal directions," Kauffman says. —Jason G. Goldman

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Good-bye Ice, Good-bye Data

Warmer temperatures in the Arctic keep archaeologists busy

Archaeologists who work in the Arctic are typically spoiled with pristinely preserved artifacts, but recently the blessing of ice has become a curse: the researchers are struggling to save the wealth of delicate material that is emerging from melting permafrost and eroding coastlines because of climate change. In northern Alaska there is only one full-time archaeologist: Anne Jensen, a senior scientist at Ukpeaġvik Iñupiat Corporation, one of the largest companies owned by Alaskan natives. Every summer Jensen excavates hard-to-access sites where Inuit people lived and hunted hundreds—even thousands—of years ago. This past summer Jensen and her colleagues returned to Walakpa, once the site of a coastal village that continues to reveal surprises because of erosion. They hope to save thousands of years' worth of cultural and environmental data from falling into the sea.

—Interview by Megan Gannon

What did you find at Walakpa this time?

Walakpa could go back 4,500 years or more. So far houses, tent platforms and various storage pits have been found. Also, people threw trash down the hill, so you have these beautifully stratified middens, which are basically garbage piles. We spent a lot of time taking faunal samples for chemical analysis and radiocarbon dating.

What's the most challenging part of being an archaeologist on the North Slope?

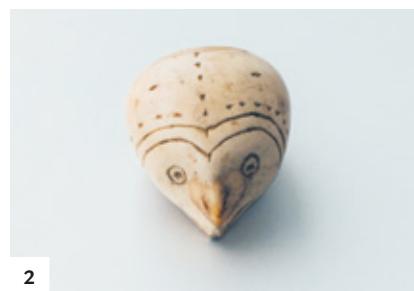
Definitely the weather. You have a fairly short excavation season—only between six weeks and two months long. The ground is frozen except for the upper layers, so after you remove the thawed materials, excavation goes more slowly.

Scientists have established that the Arctic is warming at a faster pace than the rest of the planet. How does that affect your job?

Everything has been so well preserved. Many organic remains—such as baleen strips,



1



2



3

leather goods, ivory carvings, wood bows, bone fragments and even mummies—can be 1,000 years old or more, but they look like they were buried 10 years ago. That's because they froze quickly, which slows chemical and bacterial action, and then never unfroze.

But that's changing. Climate projections are dire: some scientists say there will be no permafrost by the end of the century in locations such as Point Hope and Kivalina. Even at Point Barrow, the layer of soil that thaws during summer and freezes during winter is going to be close to six feet, which encompasses most archaeological material. That means everything is going to go through the freezing and thawing cycle every year, which is really destructive—and not just chemically. Ice crystals also mechanically deteriorate things. Plus, the sea level is rising. Plus, there's much higher risk of erosion for the coastal sites. Already across the northern coast of Alaska there are very few sites left, and many have been lost recently. Sites that people told me about 15 years ago are now gone.

Anne Jensen on-site in Walakpa Bay, Alaska (1). An ivory toggle or fastener found in 1998 in Nuvuk, Alaska (2). An ivory harpoon head discovered in 2013 at Walakpa (3).

What's at risk of being lost?

We may never be able to answer the question of how and why proto-Inuit people migrated from here to the eastern Arctic. And we're not only losing the cultural data. We basically look at the middens as frozen-tissue archives, which have a great deal of information about how ecosystems functioned at different points. Put that together with climate data and you can gradually piece together a much better understanding of ecodynamics. For example, you can figure out how walrus populations changed over time, which could inform today's hunting and conservation policies.

What could be done to protect and preserve these archaeological sites?

It's just not feasible to protect them in the long term. Ukpeaġvik Iñupiat Corporation is going to great lengths to preserve Walakpa a little longer so we can excavate more of it. But not all village corporations have the resources we do. The only option at this point is to identify the sites we think have the best preservation and the highest potential to address a lot of scientific questions and figure out a way to salvage them. They can't be preserved.

Do you have a favorite artifact that you've discovered?

A little ivory toggle or fastener from a burial at Nuvuk, at the tip of Point Barrow (2). It's a really great little owl carving. The burial date is between A.D. 875 and 1080, so assuming the owl wasn't an even older family heirloom, it is about 1,000 years old.



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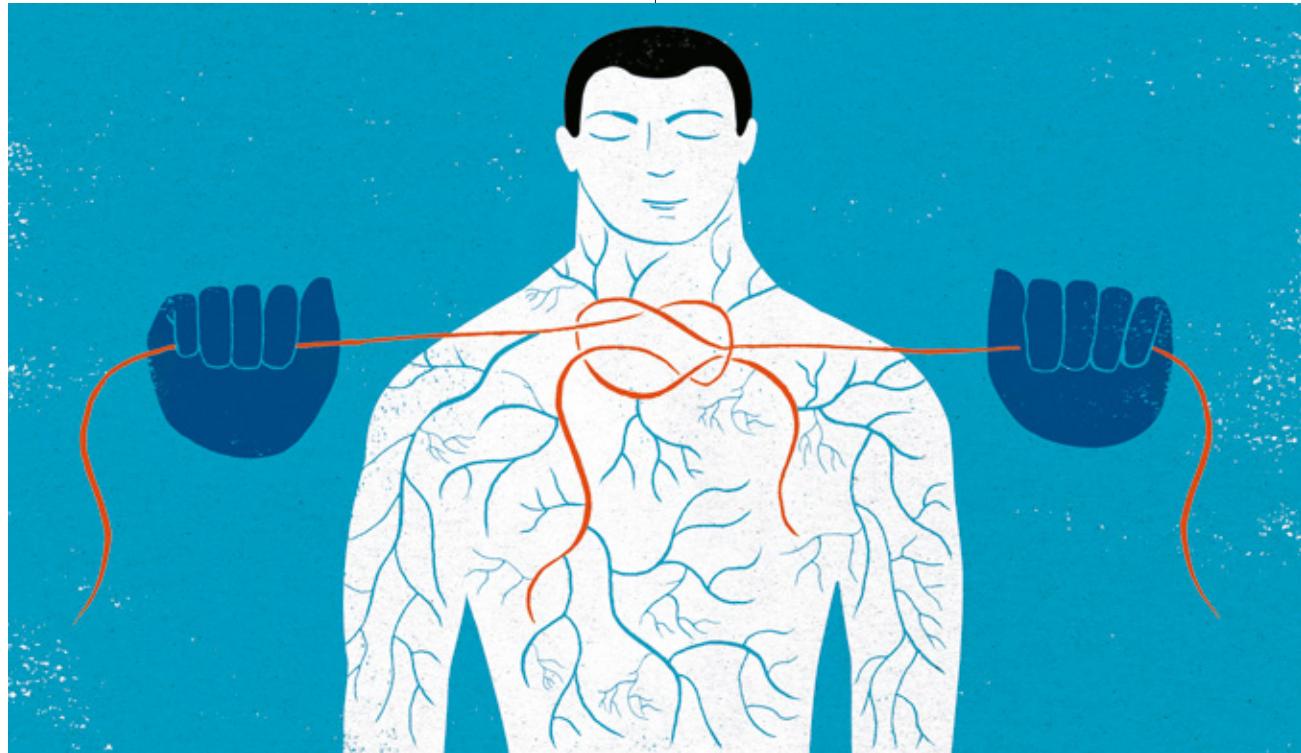
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David Noonan is a freelance writer specializing in science and medicine.



Busting Blood Clots

The go-to stroke drug often fails. Now doctors can slide out brain clots with wires and have new tools for other blockages

By David Noonan

Twenty years ago stroke doctors celebrated the arrival of a powerful new weapon: the clot-clearing drug tPA. It was hailed as a lifesaver and has proved to be one for hundreds of thousands of patients since. TPA was the first and is still the only medicine approved by the U.S. Food and Drug Administration for treating strokes caused by clots that block blood flow to the brain. But like so many medical marvels, tPA (which stands for tissue plasminogen activator) has turned out to have serious limitations. It needs to be administered within three hours of symptom onset, does not last long in the body before it loses effectiveness, can cause uncontrolled bleeding and often fails to break up large clots.

For many of the nearly 800,000 Americans who every year suffer ischemic strokes, as the brain blockages are called, these shortcomings can be deadly. Nearly 130,000 die. Sadly, there have been no good alternatives to tPA since it debuted.

Recently doctors and scientists have broken this long-standing clinical stalemate with new tools to put a dent in those grim numbers. One innovation, a tiny wire device called a stent retriever, can be snaked up into the blood vessels leading to the brain to pull out large clots. “It’s the first proven, effective treatment for acute stroke in a generation,” says Jeffrey Saver, director of the Stroke Center at the University of California, Los Angeles. Approved by the FDA in 2012, the stent retriever got a boost this year when the journal *Stroke* reported data showing many more patients treated with a retriever resumed normal life than did patients who received tPA. (The retriever manufacturer, Medtronic, provided support for the studies. Neurologist Bruce Campbell of the Royal Melbourne Hospital in Australia, who co-led the analysis, notes that *Stroke* has “strict independent-peer-review processes” to guard against bias.) Researchers are also developing better clot-detection scans, as well as a technique involving magnetism that guides tPA directly to the problem. This method could help eliminate dangerous obstructions elsewhere in the body, as well as in the brain.

BIG CLOTS, BIG TROUBLE

OF ALL OF TPA’S DRAWBACKS, the most troublesome is its inadequacy against big clots, which can block large blood vessels at the base of the brain; they cause about 25 to 30 percent of all strokes. Although it works well against smaller clots in narrower vessels, a safe dose of the drug—which is delivered intravenously—often does not last long enough in the bloodstream to dissolve the big clots, and increasing the dose raises the risk of

bleeding. “All you need to see is one intracranial bleed from tPA, and you realize you’ve got to pause before you give that medication,” says Thomas Maldonado, a clot specialist at New York University’s Langone Medical Center.

This is where the stent retriever has an advantage. It is a narrow tube that can be threaded up from the femoral artery in the leg to the site of the clot. Then wire mesh on the end of the retriever, which expands like an accordion, is pushed into the clot. The mesh tendrils keep the clot from breaking apart in the brain—which could be deadly—and help separate it from blood vessel walls. The device is next pulled out of the body, and the clot comes with it. (In years past, doctors had tried a device with a corkscrew tip but found it was not as good at clearing the clot.)

Another advantage the device has over the drug is that the time window for the use of the stent retriever after symptoms arise is double that of tPA—six hours instead of three. The *Stroke* analysis found that blood flow in a vessel blocked by a large clot was successfully restored in 236 of 306 patients, or 77 percent, treated with the stent retriever. With tPA alone, the success rate was around 37 percent.

Like all surgical interventions, the stent retriever carries the risk of complications. The main one is bleeding, which is why patients with high blood pressure and the strained vessels that go with it may not be candidates for the procedure. “There’s also a chance of the guide wire or some other manipulation of the device poking through the blood vessel during the procedure,” Saver says.

A much less common complication, Saver adds, is a piece of the clot breaking off as it is being pulled out, escaping into a new artery and causing a new stroke in a different area than the initial one. It happens in about 2 to 3 percent of cases, he says.

HELP FROM IMAGING

THE DAMAGE that blood clots do is not limited to strokes. Every year as many as 900,000 people in the U.S. develop blood clots in their legs, called deep vein thrombosis (DVT). Aside from the localized discomfort and pain it causes, DVT can travel to the lungs and become potentially lethal pulmonary embolisms, which kill an estimated 100,000 people annually. These two types of clots are usually treated with the anticoagulants heparin (for acute situations) and warfarin (for long-term problems), and surgery may be used in serious cases. The FDA approved tPA for the acute treatment of lung clots in 2002; although it carries the usual risks and complications, it can reduce the size of clots, which the anticoagulants cannot do. The drug is also gaining traction as a treatment for some cases of leg blockages.

Knowing more precisely where these clots are would help doctors go after them: location can affect choice of drugs or other treatments. Alas, current imaging methods have limitations. Existing technologies are “very good if we know where we’re looking,” says Peter Caravan, a radiologist and co-director of the Institute for Innovation in Imaging at Massachusetts General Hospital, but there is currently no single whole-body test that can spot blood clots anywhere that they might form. Ultrasound

is the first choice for finding a clot in the legs, and computed tomography (CT) scans readily detect pulmonary embolisms. CT is also the primary imaging choice for patients who arrive at the hospital with symptoms of stroke. “But if we don’t know where to look, we have to subject the patient to a battery of tests,” Caravan says, a costly and time-consuming process that can delay critical treatment.

To address the problem, Caravan and his team have invented an imaging agent that, when injected into the bloodstream, binds to fibrin, the meshlike protein that forms clots, and makes it visible to a scanner. It has potential applications for all clots, including those that cause strokes. “About a third of ischemic strokes are of unknown origin,” Caravan says. “You may think, at first, ‘So what? You had the stroke—why do you care where it came from?’ But it’s really about preventing that second stroke. Your biggest risk of having a stroke is if you’ve already had one.”

Because the experimental probe binds to fibrin (and “lights up” in a positron-emission tomography scan), it can help establish how dangerous a clot is: younger clots, which have more fibrin than older ones, are less stable and more likely to travel to the lungs. They can also make it up to the brain, triggering a stroke. Further, tPA is more effective against fibrin-rich young clots than it is against older clots, and so the probe could help determine which clots to attack with the drug. After a series of animal experiments, researchers began safety testing of the new agent in healthy human subjects this past spring.

Some doctors think that tPA could work faster and prevent strokes more successfully if the drug could be guided swiftly and efficiently to the clot rather than simply being injected into the bloodstream. Researchers at Houston Methodist Hospital are experimenting with a way to transport tPA to the clot while protecting it from the body’s defenses, which degrade the drug. They are experimenting with iron oxide nanoparticles, stuffed with tPA and “biochemically camouflaged” with a coating of the naturally occurring blood protein albumin. The albumin jacket fools the body’s defenses and gives the tPA extra time to work on the clot; the iron oxide enables monitoring with magnetic resonance imaging, remote guidance of the nanoparticles with external magnetic fields and magnetic heating at the site to accelerate clot dissolution. And because the tPA does not degrade while it is being ferried to the clot inside the iron oxide, the dose can be smaller, reducing the risk of hemorrhage. Results with human tissue cultures and animal models have been promising, and clinical trials in humans are planned.

Of course, stopping blood clots from forming in the first place would be even better. There is a growing list of clotting conditions caused by genetic mutations, and researchers around the country, including a team at N.Y.U. Langone, are analyzing the role that genes play in clots. “That’s the genetic handprint we’re looking for,” Maldonado says. The goal is to develop a genetic test that would show if a person is at increased risk and to offer preventive treatment such as an anticoagulant. This approach could hinder the blockages, making elaborate feats with wires and magnets unnecessary. ■



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

The Bright Side of Internet Shaming

It's become so common that it might soon begin to lose its impact

By David Pogue

Brian Williams. Anthony Weiner. Social media mogul Sean Parker. Plagiarist Jonah Lehrer. Walter Palmer, the dentist who shot Cecil the lion. The woman who sued her nephew in Connecticut for knocking her down with a hug at his eighth birthday party. The tourist who gave the finger to a “Silence and Respect” sign at Arlington National Cemetery. The woman who tweeted, “Going to Africa. Hope I don’t get AIDS.”

By now everyone knows about Internet shaming. Someone makes a mistake in judgment—or *seems* to because the story is repeated without context—and it goes viral. The public responds on Twitter and Facebook with a bombardment of vitriol, threats and humiliation and, often, an attempt to destroy the person’s job, home and family.

“Lowlife c***. I’d love to smash your teeth in,” goes the typical tweet. “I’d put a cross bow bolt through Walter Palmer then track



him [for] 40 hrs, shoot him, behead him, skin him and sleep peacefully.” When the victim of shaming is female, the tweets are often sexually violent: “Somebody (HIV+) must rape this b**** and we’ll see if her skin color protects her from AIDS.”

Because of their immensity and anonymity, these floggings feel infinitely worse than, say, being booed off a live stage. It feels as though the entire world has judged you, found you worthless. Then it gets worse. The mob starts working to destroy your life.

In 2012 Adam Mark Smith accosted a Chick-fil-A clerk for working for a company that supports hate groups. When the video hit YouTube, the mob filled his employer’s voice mail with bomb threats; he lost his job within 24 hours.

“I’d get voice mails and … texts [saying] ‘You deserve to die. I hope you lose your kids. You … are … a horrible human being,’” Smith told me in an interview for CBS News. They nailed a swastika to his front door. They mailed him a package full of human feces. They posted the address of his young children’s elementary school, with directives to harass them. Smith had to move.

One potential employer after another withdrew their job offers. He wound up on food stamps. He contemplated suicide.

In his 2015 book *So You’ve Been Publicly Shamed*, Jon Ronson makes it clear that public shaming isn’t new. We used to put wrongdoers in the stocks in the public square or, centuries before that, stone them. The anonymity and speed of the Internet, of course, just make shamings easier to start, execute and coordinate.

Any reasonable person would agree that, for a politically insensitive act or tasteless joke, permanently ruining someone’s life is too harsh a penalty. But these days public shamings are increasingly frequent. They’ve become a new kind of grisly entertainment, like a national reality show.

The truth is, the cybermob phenomenon won’t go away. Human nature is what it is. Psychology is at play. When they can’t see their victims, people tend to be far more vicious than they would be face-to-face (the online disinhibition effect). And even if some people might be inclined to defend the victim or add some context, they don’t, because they don’t want to get in the cross fire (the bystander effect).

Yet in a twisted way, there’s a certain kind of hope in the increasing regularity of shamings. As they become commonplace, maybe they’ll lose their ability to shock. The same kinds of ugly tweets have been repeated so many times, they’re starting to become boilerplate.

If you’re a target, it’s not actually about you. You’re a symbol, a faceless bull’s-eye for the frustrations of your attackers. Furthermore, you’re only the hate symbol du jour; the Internet’s sights will be on someone else next week. And as time goes by, the novelty wears off, and the pattern becomes predictable, then maybe it will be easier for victims to accept that at least an Internet shaming isn’t personal. In the end, it’s just a sport. ■

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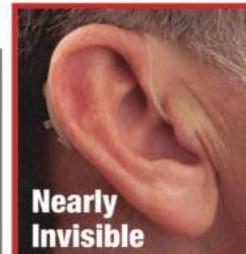
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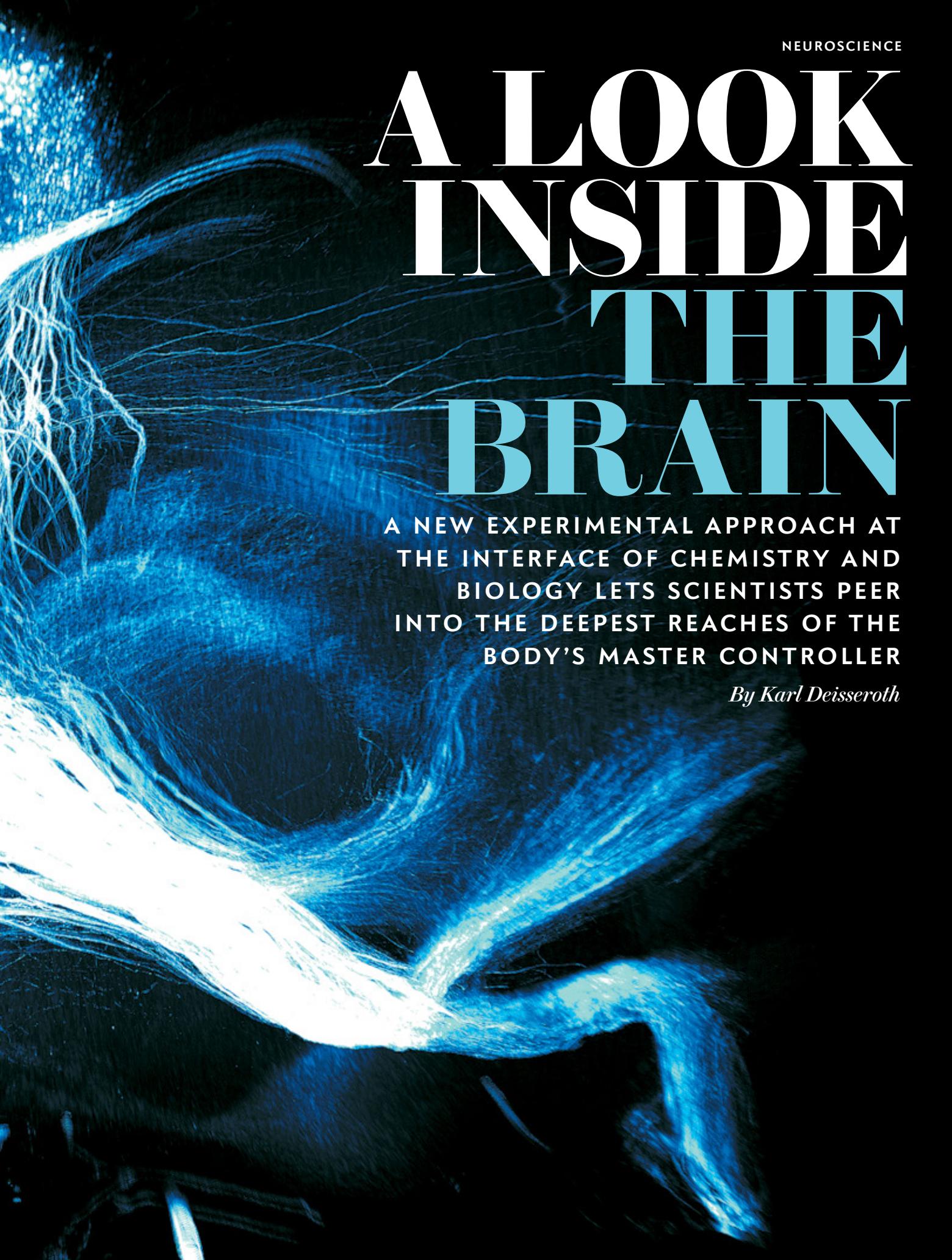
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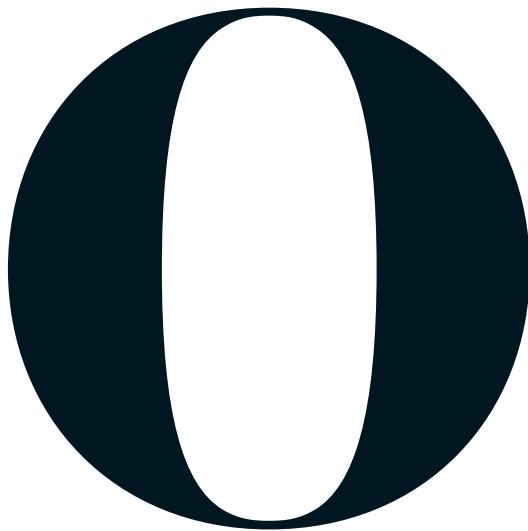
GLOBAL VIEW of fibers extending out from cells in the frontal area of a mouse brain demonstrates the benefits of a hydrogel-embedding method that allows researchers to trace the complexities of neural wiring.



A LOOK INSIDE THE BRAIN

A NEW EXPERIMENTAL APPROACH AT
THE INTERFACE OF CHEMISTRY AND
BIOLOGY LETS SCIENTISTS PEER
INTO THE DEEPEST REACHES OF THE
BODY'S MASTER CONTROLLER

By Karl Deisseroth



the brain's own version of crossing, or "weft" fibers: axons that wind back and forth over short distances, transmitting signals to perform computations.

To understand the inner workings of the brain, scientists need to decipher how this neural tapestry is organized at the level of individual elements, such as an individual axon. But to understand the role of an axon, we would also like a global perspective spanning the entire brain that somehow does not lose sight of the single, threadlike axon and its context. To gain such a view, one needs a special kind of tool because the brain is not flat like woven cloth, nor is it transparent. Fat molecules (lipids) throughout the brain, particularly in cell membranes, cause light from imaging devices to scatter and thus greatly hinder our view beyond the most superficial layer of cells into the profound depths of the brain.

Now a new technology has opened exciting vistas for neuroscientists, creating a way to see into the intact brain—and to both determine the trajectories and define the molecular properties of individual connecting fibers that weave through the brain's intricate inner workings. This method is built on the chemistry of hydrogels, polymers that form a three-dimensional network of connected compartments able to retain water

without dissolving. It is used to create 3-D polymer endoskeletons within biological tissue. In this three-step process, a transparent gel is first formed within the laboratory animal or postmortem human brain itself, linked to and thus protecting the brain's key information-rich molecular parts, including proteins and nucleic acids (DNA and RNA). This step is followed by the removal of the tissue components that are not of interest or that scatter light, such as lipids. Finally, by introducing a multitude of fluorescent labels and other markers throughout this structure—in addition to being transparent, the gel is designed to allow fast infusion of these probes—scientists can light up and directly visualize diverse fibers and molecules of interest at very high resolution throughout the intact brain.

This newfound ability to see into the depths of the body's master controller is leading to numerous insights. Scientists are using this approach to link physical form with behavioral function of neural pathways involved in action and cognition, ranging from movement to memory. This method has also helped elucidate processes that contribute to parkinsonism,

Karl Deisseroth is a professor of bioengineering and psychiatry at Stanford University. He was the recipient of the 2015 Lurie Prize in Biomedical Sciences for the development of CLARITY and optogenetics.



IN BRIEF

The brain's inner workings will only yield themselves to neuroscientists through close inspection of individual cells combined with large-scale surveys of the entire organ.

Optical imaging methods in routine use cannot penetrate the opaqueness of brain tissue because of light scattering at the interfaces of water and the fat molecules in cell membranes.

New techniques that remove lipids and replace them with a substance that holds brain parts in place furnish a window to gaze past the typical barriers that block an internal view.

Hydrogel-embedding methods, as these techniques are called, allow researchers to examine the wiring of specific neural circuits that control various behaviors.

Alzheimer's disease, multiple sclerosis, autism, drug abuse, and fear and anxiety disorders. We even helped start a company to explore tissue-hydrogel applications for cancer diagnosis. This method is now being applied beyond the brain to diverse organs and tissues across the entire body.

GOING CLEAR

MAKING A SEE-THROUGH BRAIN is so difficult that even evolution, over hundreds of millions of years, has not achieved that feat in the lineage of large animals. Invisibility, of course, could provide major advantages, and some species have been evolutionarily selected for a certain amount of transparency to adapt to their environment (for example, to avoid predators). Certain fish even lack the reddish hemoglobin protein, essentially doing without blood as most vertebrates know it and thus achieving a modicum of invisibility. Yet even these animals cannot seem to make their central nervous systems transparent, despite intense evolutionary pressure. In partially transparent fish or shrimp, nervous systems remain at least partially opaque; evolution can go even as far as giving up on red blood cells, but nothing, it seems, lets light move unimpeded through a large living brain.

This opaque quality results from light being scattered in neural tissue. Photons bounce off interfaces of fat and water (because of differences in the rate at which light travels in the two substances) and in seemingly random directions (because of the structural complexity of neural wiring). This effect cannot be easily engineered or evolved away. The lipid barriers that constitute cell membranes and internal structures within a brain cell also play key roles as insulating material for the ions that mediate the flow of electrical impulses along intricately intertwined axons. Ironically, the organ that biologists most need to keep intact to understand is also the one that we have been least able to render transparent.

In 2009 I turned to the unresolved challenge of making the intact, mature, mammalian brain transparent—while still allowing detailed labeling of diverse molecules within. By then, hundreds of labs around the world had begun using a technology my colleagues and I had developed between 2004 and 2009 for turning specific brain circuit components off and on with light. The technique, called optogenetics, combines lasers, fiber optics and genes for light-sensitive proteins called microbial opsins from algae and bacteria to control neural activity precisely in specific cells within whole living brains as animals run, jump, swim, socialize and carry out complex behaviors. By the summer of 2009, five years after the initial July 2004 experimental demonstration with microbial opsins in neurons, key challenges in optogenetics were largely resolved, and the technique could be easily and generally applied. Although thousands of new insights on the causal neural mechanisms of behavior have since been discovered with this method, optoge-

netics alone cannot provide another key type of information: a high-resolution picture that furnishes insight into the brain-wide wiring of the individual cells being controlled by light.

Linking the big picture of a system to its individual basic components is an aspiration common to many fields of science, although this goal often (and appropriately) gets sacrificed. Separating out the individual parts of a complex system for isolated analysis has always been essential to science because removing a component from its context allows one to determine which properties are intrinsic and do not depend on other elements. But for a richly interconnected structure such as the brain, taking the system apart, like separating all the threads of a tapestry, is not always the best strategy for understanding and appreciating the big picture.

For visualization and labeling, the opaque nature of adult mammalian brains had long dictated the necessity for disassembly, typically via slicing the brain, thus turning the three-dimensional volume of tissue into hundreds or thousands of

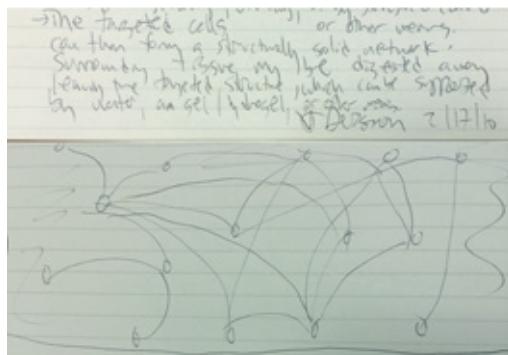
virtually two-dimensional slices. This process consumes prohibitive amounts of time and expense, especially when many brains are required to produce meaningful statistical results (as is common in the study of mammalian behavior). Moreover, key information is irreversibly lost. Because, with optogenetics, we were already building new functionality within the intact brain, in 2009 I began to consider what else we could build within a brain to help us with this problem.

The seed of the idea had been planted 15 years earlier. In the mid-1990s I had become intrigued with the idea of trying to build brainlike circuits in the lab, start-

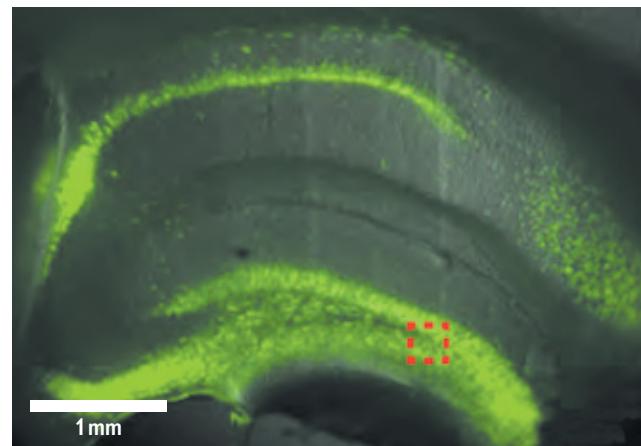
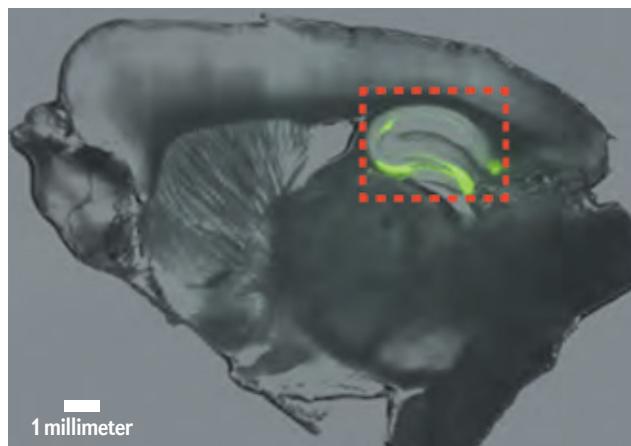
ing from individual cells. One way to do this might be by seeding neural stem cells onto polymer scaffolds, where they could be biochemically coaxed to turn into neurons. In pursuing this effort, I had delved into the science and engineering literature of hydrogels that appeared to be particularly appealing as scaffolds by virtue of their biocompatibility and transparency.

In later years I would eventually carry out only simple pilot experiments, seeding stem cells onto polymeric scaffolds and turning them into neurons, but I never got to the point of making an intact brainlike structure from single cells—a devilishly challenging undertaking. Still, I dutifully lugged my increasingly dusty folder of carefully stapled papers labeled “hydrogels” as I moved from lab to lab during the next 15 years and from step to step in my career (receiving my Ph.D. in neuroscience in 1998, completing my psychiatry residency and postdoctoral fellowship, and launching my engineering lab at Stanford University in 2004). But the mental scaffolding was in place, and the idea took root and eventually evolved, with the critical involvement of some amazingly talented people in the lab, into a workable strategy for building a transparent and accessible brain.

A sketch I made in February 2010, while sitting at my desk



INITIAL SKETCH in the author's lab notebook in early 2010 traces the idea for building a hydrogel in tissue and removing other components.



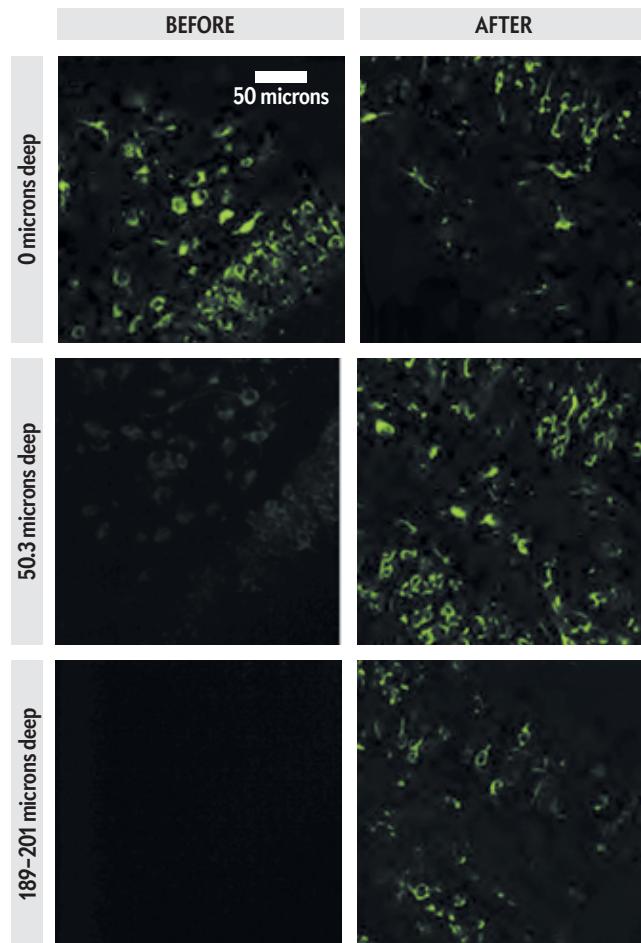
after a long period of considering the problem of brain-wide visualization, depicted the basic idea [*see illustration on preceding page*]. It was the initial concept turned on its head—instead of starting from a hydrogel and building a brain within, we would start from a brain and build a hydrogel within. The hydrogel would serve as a support structure and preserve spatial placement of brain components we cared about, such as proteins and nucleic acids, but allow removal of everything else that kept us from seeing deep within. It would, meanwhile, prevent the brain from collapsing into a shapeless soup as structural but less interesting components were dissolved or digested away.

The very first experiments, which bridged separate fields and brought initial tentative shape to what had been mere possibility, can be best appreciated years later with the broad perspective that passage of time brings. Two creative and courageous researchers then at the lab—Viviana Gradinaru and lab manager Charu Ramakrishnan—were the first ones willing to take on this daunting project. The risk of failure was so high that I decided not to involve the whole group; I thought that these two experienced researchers (who had been very successful already with other projects) could handle the risk and disappointment if the project ultimately did not work out.

Beginning in early 2010, Gradinaru and Ramakrishnan sought to make neurons invulnerable to damage from the agents that would disrupt fine tissue structure and cell membranes. In theory, filling brain cells with a durable polymer of some kind might do the trick, and the neurons would then remain intact if supported by the hydrogel. The two tried a number of strategies, including the introduction of genes encoding certain enzymes to allow neurons to manufacture durable polymers such as chitin and cellulose. The best approach, a creative idea from Gradinaru, turned out to be a process to make another biopolymer, keratin, inside cells. She had shown that keratin in cultured neurons could protect cell structure from disruption and reasoned that for intact brain tissue (with the neurons stabilized with keratin and hydrogel added for external support) the lipids might be washed out with detergent to reveal the targeted brain structures of interest, suspended in the transparent hydrogel.

At that point, building the hydrogel in the intact brain existed as a pure idea. I decided to make the project move more quickly by seeking deeper experience from a chemical engineer. Although no

MOUSE BRAIN embedded with a transparent hydrogel—after removal of light-scattering tissue—glows green when a fluorescent protein linked to keratin illuminates marked cells. Zooming in from a view spanning the brain (*upper left*), the curves of the hippocampus substructure (*upper right*) appear, followed by close-ups of individual cells (*lower panels*). Prior to implementing the CLARITY process, cells at a depth of more than 50 microns from the surface were invisible because of light scattering (*left panels below*). Once the process is complete, as shown in this 2010 experiment from Viviana Gradinaru, Kwanghun Chung and Charu Ramakrishnan, cells can be detected to depths of around 200 microns or more (*right panels*).



COURTESY OF DEISSEROTH LAB, STANFORD UNIVERSITY AND VIVIANA GRADINARU, KWANGHUN CHUNG AND CHARU RAMAKRISHNAN

one outside the lab knew of the project, I searched my in-box for e-mails from prospective postdoctoral fellows who might have the right background in hydrogels. The name of Kwanghun Chung, a remarkably talented chemical engineer, then at the Georgia Institute of Technology, came up. Chung had heard of our optogenetics and stem cell work and was interested in joining the lab.

In early March 2010, only a few weeks after making my original sketch shown in the illustration on page 33, I set up our first brief conversation over the phone while I was at a meeting in Utah. Then I did something that I had never done before (or since) because I was so sure about this new direction. I invited Chung to join our team without even a lab visit or face-to-face interview. Strange times for a neuroscience lab—a chemical engineer appearing out of nowhere.

On his arrival, Chung launched immediately into the under-the-radar project. By the end of 2010 the three-member team in my lab had created transparent blocks of a mouse brain in which the preserved keratin-containing and hydrogel-embedded cells could be seen clearly, even hundreds of microns deep within tissue, a far greater depth than would have been possible using existing methods [*see illustration on opposite page*]. The first fully functional hydrogel that Chung produced was based on acrylamide, commonly used in the lab to separate nucleic acids or proteins. The gel-tissue hybrids produced from this creative work were designed so that we could introduce fluorescent markers and other labels directly to visualize preserved proteins and structures, such as axons, over many rounds of labeling, and we found that we no longer needed a keratin component to keep cellular structures in place—the hydrogel alone was enough. Despite pioneering work with other approaches from Hans-Ulrich Dodt and Atsushi Miyawaki (the 3DISCO and Scale methods, respectively), such transparency and accessibility in the adult mammalian brain had not been previously achieved.

This particular acrylamide-based variant of the hydrogel-built-in-tissue idea (there are now many other published variants) was named CLARITY (for clear *lipid-exchanged acrylamide-hybridized rigid imaging/immunostaining/in situ hybridization-compatible tissue-hydrogel*). Since our 2013 publication of the technique, even this single version of the tissue-hydrogel technique has been adopted for diverse basic science applications and also applied clinically (for example, to postmortem brains of individuals with autism or Alzheimer's), as well as to spinal cords and brains of mice (for example, in discovery of previously unknown pathways for control of fear and anxiety behavior). Many papers from labs around the world have now been published using this general approach to understand the basic structure of the nervous system, often in combination with optogenetics, and to provide fresh ideas for understanding adaptive and maladaptive brain circuitry.

Just as the first five years of optogenetics with microbial opsins brought forth numerous innovations enabling broad applicability of that method, the technique for building tissue-hydrogels inside

brains has likewise advanced dramatically over the first few years of that method's existence. For example, the earliest version of the hydrogel technique described a step with an imposed electric field to accelerate rapid clearance of electrically charged detergent particles bound to lipids. This step took some practice to master, and tissue could be damaged if the voltage had been turned up too high. To tackle this issue, beginning in early 2014 Raju Tomer, Brian Hsueh and Li Ye, all then lab members, published two papers (one co-authored with our colleagues in Sweden) defining a simplified version of this step. It became known as passive CLARITY because it does not use electric fields. Tomer and the team also described specialized brain-hydrogel imaging using a high-resolution fast form of light sheet microscopy, adapted to the unique challenges of rapidly imaging large hydrogel volumes by scanning planes—light sheets—instead of points of light.

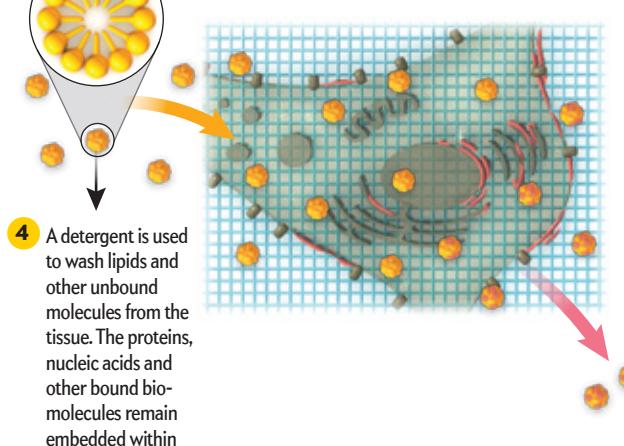
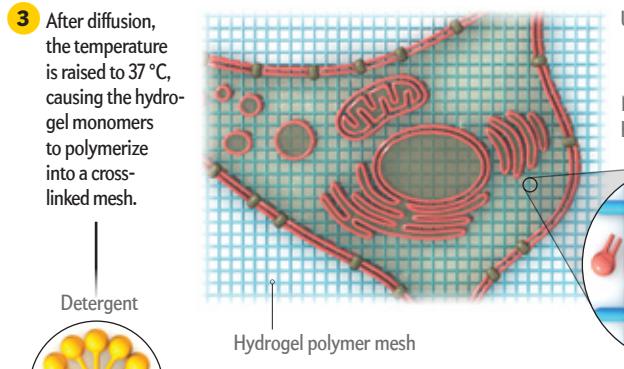
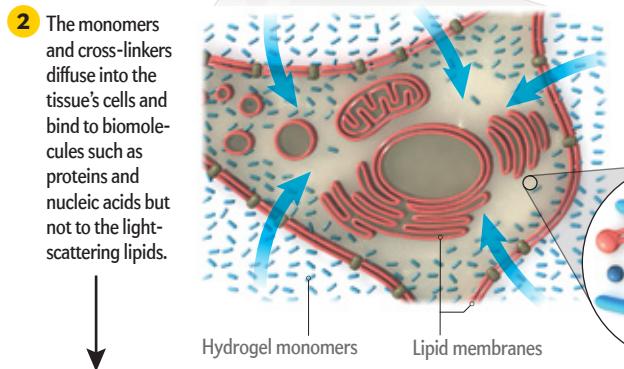
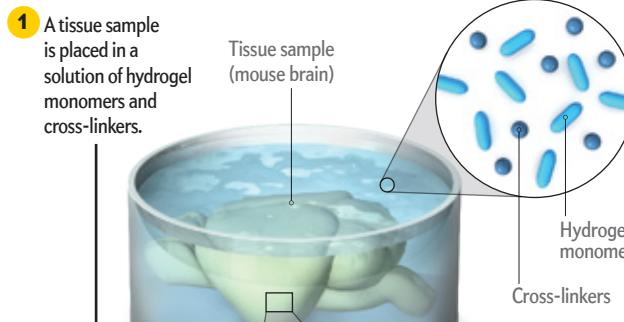
Gradinaru and Chung were both running their own thriving labs at this point (at the California Institute of Technology and the Massachusetts Institute of Technology, respectively), each gener-

Tissue-hydrogel techniques enable access to the brain's deepest reaches, giving insight into the biology of the brain and its disorders.

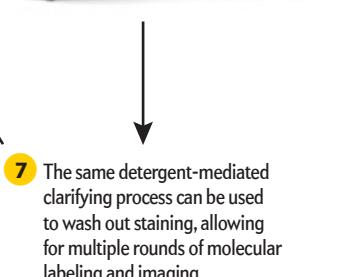
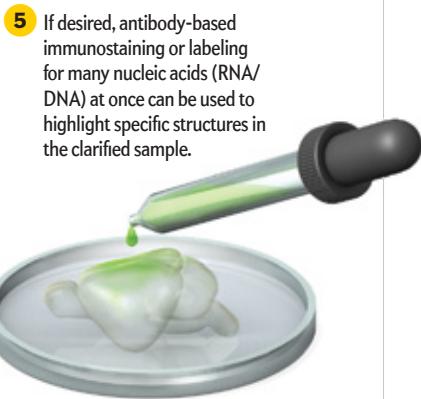
ating major new innovations. Indeed, subsequent developments have come quickly not only from these but also from many other investigators. Gradinaru independently developed and published a CLARITY strategy suited for whole organisms called PARS. Both Gradinaru and Chung published new hydrogel formulations called PACT and SWITCH, respectively, and now a large variety of tissue-hydrogel composites have been described from labs around the world. Yet when it comes to exploring possible hydrogels experimentally, we have only scratched the surface. In 2013 Chung and I disclosed a very long list of possible hydrogel variant compositions, from acrylates to alginates and beyond, and my lab and our collaborators are now exploring ways in which the polymers can even become active—modified, for example, with elements that could create tunable electrical conductivity or chemical reactivity, opening up new possibilities.

Another challenge related to a property of tissue-hydrogel composites, which, as we described in our 2013 and 2014 papers, causes the hydrogel-embedded tissues to physically expand substantially. This property of the composite is not always a problem and can be compatible with imaging at high resolution, either in the original CLARITY or in later, similar hydrogel-in-brain formulations (each with its own identifying acronym: PACT/ePACT

Making a Tissue-Hydrogel



Cursory sketches of a technique for making a brain transparent gradually evolved into a new chemistry-based method for creating a novel kind of material, a tissue-hydrogel hybrid that stabilizes neurons and molecules within the intact brain before removing lipids in cell membranes that prevent researchers from getting an unimpeded view. Many such hydrogel-embedding methods are now being adopted in neuroscience laboratories globally to study intact tissue in ways that were until now impossible.



beginning in 2014, followed in 2015 and 2016 by ExM/proExM and MAP) developed by other groups that promote the basic swelling effect. But to be able to compare our transparent brains with those in academic brain atlases, which requires a precise, undisturbed rendition of the original tissue, we developed a final, optional step for shrinking enlarged tissue back to original size.

With Ye and another team member, Will Allen, my lab also developed and published high-speed and automated imaging and analysis software that can be downloaded and used by anyone. The group of our colleague Marc Tessier-Lavigne, then at the Rockefeller University and now president of Stanford, did so as well for its new iDISCO method. These two complementary papers were published in the same issue of *Cell* just this year. My group, including Emily Sylwestrak, Priya Rajasethupathy and Matthew Wright, has also been able to make a crucially important type of fluorescent labeling of many RNAs at once work reliably within intact brains using yet another tissue-hydrogel formulation, as we earlier reported in a *Cell* paper in March.

The ability to label multiple types of molecules, including nucleic acids such as RNA, turns out to be a special advantage of the hydrogel approach and opens up vast realms of gene-expression analyses. With all these challenges resolved—many of them only this year—the technique has now matured to where it is used by labs across the world.

BRINGING THE THREADS TOGETHER

IT IS REMARKABLE to look back and compare the initial humble sketch in 2010 with its fully functional implementation and integration just six years later [see illustration on pages 30 and 31]. A key goal driving this progression of the tissue-hydrogel vision has been to complement intact-brain optogenetics with intact-brain structural information—a goal already realized and reported on in several papers, including one in the June 16 issue of *Cell*. The work described in that paper focused on the brain's prefrontal cortex, a region responsible for regulating high-level cognitive processes and emotions. Scientists hope that understanding how this structure controls such diverse behaviors may provide insight into psychiatric disorders such as autism and schizophrenia.

With Ye, Allen and Kim Thompson, all then in my group, along with colleagues in other labs, including those of Liqun Luo and Jennifer McNab, both at Stanford, my team first used optogenetics to define a cell population in the prefrontal cortex that is active during (and also controls appropriate behavioral responses to) rewarding experiences such as highly palatable food or even cocaine. We next found a complementary population of prefrontal cells for negative (aversive) experiences. And finally, using our latest tissue-hydrogel methods, we were able to show that these two different populations of cells each wire up differently across the brain—the positive ones preferentially

send connections to a deep-brain structure called the nucleus accumbens [see illustration on pages 30 and 31], whereas the negative ones are more connected to a deep structure called the lateral habenula. In this way, the tissue-hydrogel and optogenetic approaches are allowing scientists to study intact biologi-

After creating a transparent brain, our group could look at an area called the prefrontal cortex and see how cell populations for positive and aversive experiences were wired differently.

cal tissues in consequential ways never before possible and to make headway in understanding the basic biology of health and disease.

The fullest appreciation of complex systems emerges with the ability to exchange information at both local and global scales, whether the system in question is a whole brain or an intricate tapestry. In neuroscience, enormous amounts of data can now be collected with rich and diverse detail illuminating intact-organ structure, molecular components and cellular activity. As a result, a broad yet nuanced perspective on brain function is starting to take shape.

Achieving such global perspective with local resolution is difficult—and uncommon—but it is important to meet this challenge. Emergent properties of complex systems often arise from local interactions, like the weave of a tapestry and like the process of science itself. Only with a sweeping perspective does the role of each kind of thread become clear. ■

MORE TO EXPLORE

Methods and Compositions for Preparing Biological Specimens for Microscopic Analysis. Filing date: March 13, 2013. www.google.com/patents/US20150144490

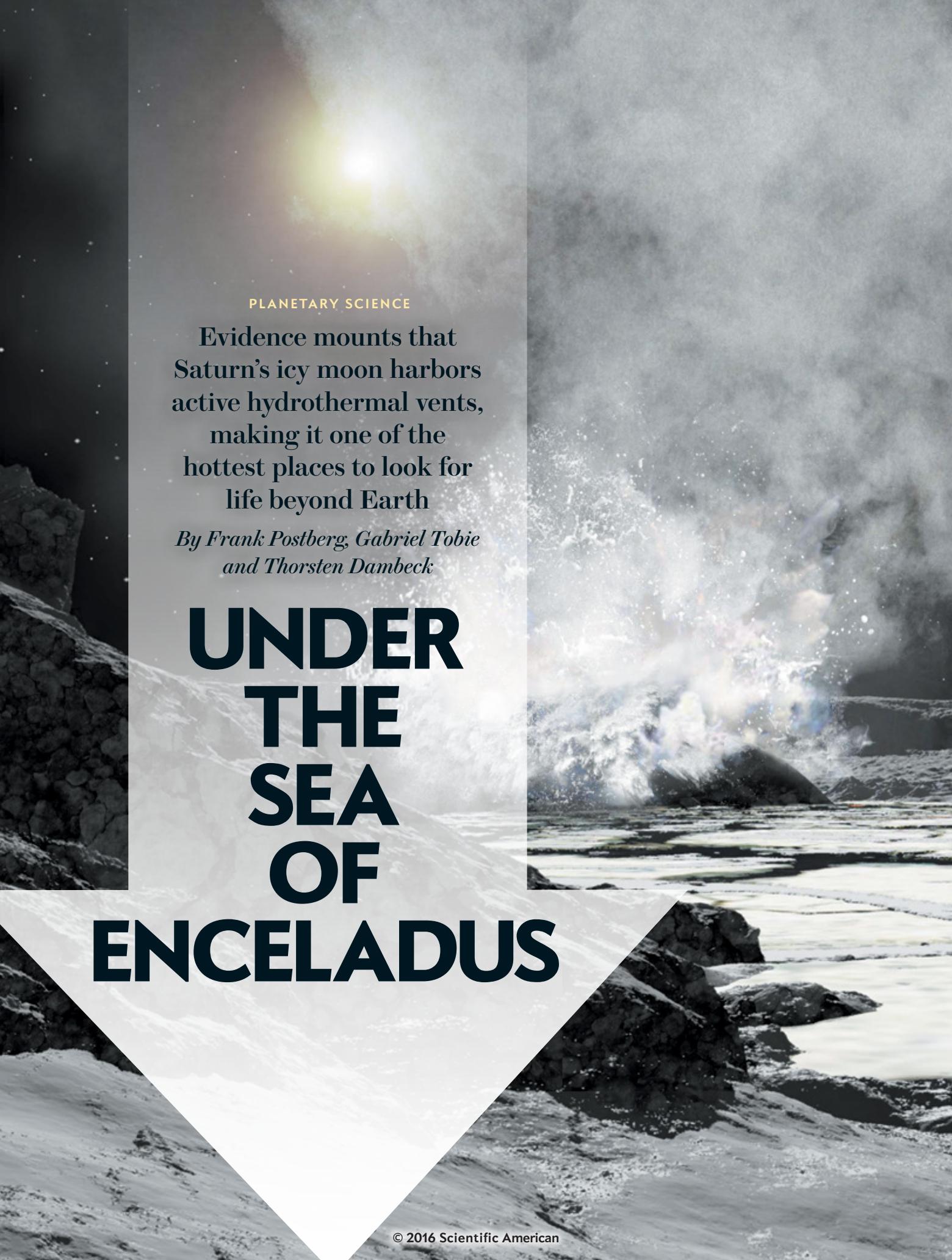
Structural and Molecular Interrogation of Intact Biological Systems. *Nature*, Vol. 497, pages 332–337; May 16, 2013.

Optogenetics: 10 years of Microbial Opsins in Neuroscience. Karl Deisseroth in *Nature Neuroscience*, Vol. 18, No. 9, pages 1213–1225; September 2015. www.ncbi.nlm.nih.gov/pmc/articles/PMC4790845

CLARITY Resources Web site: clarityresourcecenter.org

FROM OUR ARCHIVES

Controlling the Brain with Light. Karl Deisseroth; November 2010.



PLANETARY SCIENCE

Evidence mounts that
Saturn's icy moon harbors
active hydrothermal vents,
making it one of the
hottest places to look for
life beyond Earth

*By Frank Postberg, Gabriel Tobie
and Thorsten Dambeck*

UNDER THE SEA OF ENCELADUS





T

HE BOTTOM OF THE NORTH ATLANTIC OCEAN MIDWAY BETWEEN BERMUDA AND THE Canary Islands must rank highly on any list of unlikely places to find a bustling city. Yet there, in the darkness that reigns nearly a kilometer below the sunlit surface, nature has built an undersea metropolis, a complex of limestone towers as tall as skyscrapers that is home to masses of snails, crabs and mussels. The towers form as minerals precipitate out of warm alkaline water jetting from hydrothermal vents along the ocean floor. Biologists using submersibles and remote cameras found this exotic “Lost City” in the early 2000s and have been studying it ever since to learn how hydrothermal vents can sustain thriving ecosystems so far from the life-giving light of the sun. In the meantime, planetary scientists using the Cassini space probe have made a revolutionary series of related discoveries in the outer solar system, finding strong evidence that hydrothermal vents much like those of Lost City exist not only on Earth but also in the mysterious subsurface ocean of a small, icy Saturnian moon called Enceladus. Could life exist there, too?

Naturally, the possibility of extraterrestrial life tantalizes scientists, but they would have been excited about otherworldly hydrothermal vents even without aliens dangling in front of their eyes. The same evidence that suggests hydrothermal activity on this faraway moon is also providing critical information about the composition and longevity of Enceladus’s ocean. Those secrets might otherwise be forever hidden underneath a frozen crust, as they might be for other ocean-bearing moons currently lacking strong evidence for hydrothermal activity, such as Jupiter’s Europa.

More fundamentally, the very existence of Enceladus’s hydrothermal vents poses an irresistible puzzle. Other than water, the most important ingredient for hydrothermal activity is obviously heat, but this icy moon’s sizzling innards are not easily ex-

Frank Postberg directs the evaluation of the mass spectra from Cassini’s Cosmic Dust Analyzer. Similarly at home in planetary science, physics and chemistry, he is active both at Heidelberg University and at the University of Stuttgart in Germany, where he studies cosmic dust and icy moons.



Gabriel Tobie is a French planetary scientist who began studying the interiors of icy moons after growing up inspired by NASA’s Galileo mission to Jupiter. He now develops models to understand how tidal friction could power the activity of Europa, Enceladus and other icy moons.



Thorsten Dambeck is a German physicist and science writer who focuses on astronomy and planetary science. He first glimpsed Enceladus through a telescope as a youngster in the early 1980s, when Saturn’s rings were edge-on, and the tiny moon appeared as a faint white dot.



plained. Enceladus is roughly the diameter of England—relatively runty for a moon and far too small to hold onto the primordial heat left over from its formation. Some other source of warmth must be at work deep within. Learning how Enceladus generates and sustains its toasty interior could revolutionize our understanding of icy moons—and their prospects for life.

FIRST HINTS

SCIENTISTS BEGAN TO SUSPECT an ocean within Enceladus in 2005, about a year after Cassini’s arrival in the Saturnian system, when the spacecraft observed a huge plume of water vapor and ice grains rising hundreds of kilometers into space from tectonically active terrain around the moon’s south pole. In a series of subsequent flybys, Cassini traced the plume to multiple jets emanating

IN BRIEF

Data from the Cassini orbiter show that Saturn’s icy moon Enceladus has a subsurface ocean venting a plume of seawater into space. The plume provides a glimpse of the moon’s deep interior.

Studies of the moon and its plume have helped researchers estimate the temperature and composition of Enceladus’s ocean and have revealed evidence of hydrothermal vents on the seafloor.

On Earth, hydrothermal vents support ecosystems and may have nurtured life’s origins. The potential for life on Enceladus depends on the age and longevity of its ocean and hydrothermal activity.

Enceladus’s ocean and hydrothermal activity can last only as long as its supply of internal heat. Future missions could clarify this heat source and even make the first discovery of life beyond Earth.

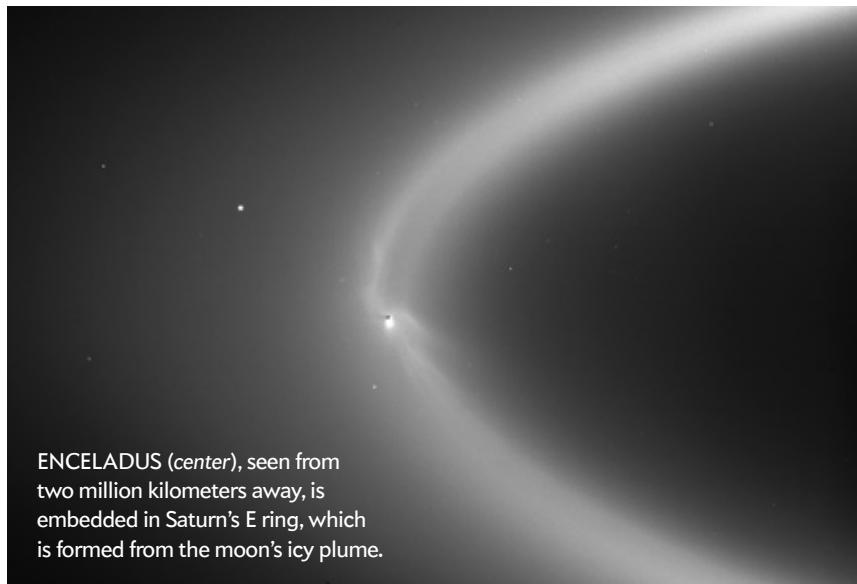
nating from four linear fissures so much warmer than their frigid surroundings that they glowed in infrared. Mission scientists called the fissures “tiger stripes” and pinpointed their jets as the source of the tenuous, sprawling ring of icy particles—known as the E ring—that encloses Saturn’s classical ring system. Most of the jets’ ice grains, however, travel too slowly to reach this ring and instead fall back to Enceladus as a fine-powdered snow. Based on the 100-meter-high snowdrifts that cover parts of its southern hemisphere, researchers estimate that Enceladus has been venting water into space for 10 million years or more.

Although the “ocean hypothesis” for Enceladus’s jets was initially controversial, an extended series of studies by Cassini has now irrefutably confirmed that a global deep sea hides inside the moon.

Most recently, an analysis of Enceladus’s gravitational field, surface topography and slight rotational wobble by Ondřej Čadek of Charles University in Prague and his collaborators, including one of us (Tobie), placed the best yet limits on the ocean’s size and extent. Their work suggests that the crust must be about 35 kilometers thick near Enceladus’s equator but less than five kilometers thick in and around the south pole. The ocean floor would lie about 70 kilometers under the surface, which would mean Enceladus’s sea holds about a tenth as much water as the Indian Ocean. And based on data gathered by Cassini in 2009 and 2011, one of us (Postberg) has shown that the water is alkaline and salty, containing sodium chloride—standard table salt—in its ejected plume. This means the ocean most likely lies atop (and leaches minerals from) the moon’s rocky core.

The crucial evidence for the presence of hydrothermal vents was gathered beginning in 2004 by Cassini’s Cosmic Dust Analyzer (CDA), before the spacecraft even arrived at Saturn and discovered Enceladus’s plume. As Cassini approached Saturn from interplanetary space, unexpected showers of microscopic, fast-moving nanoparticles struck the CDA like buckshot. Years later, after the discovery of the plume, Postberg examined the distribution of the nanoparticle sizes and frequency in the CDA data, finding none of them to be larger than 20 nanometers and all of them to have a composition most consistent with that of essentially pure silicon dioxide—silica, the main constituent of quartz rock and beach sand. Using numerical simulations to trace the most probable trajectories for the silica nanoparticles, Hsiang-Wen Hsu of the University of Colorado Boulder surmised that they had originated in the outer reaches of the E ring. Because we knew that Enceladus produces the E ring, this finding strongly suggested that the nanoparticles had come from the icy moon. Their composition proved to be the smoking gun for discovering Enceladus’s hydrothermal activity.

Pure silica jetting from Enceladus was a surprise because its only plausible source would be deep underneath the ice and the ocean, in the moon’s rocky core, where silicon mostly exists in minerals chemically bound with other elements such as iron



ENCELADUS (center), seen from two million kilometers away, is embedded in Saturn’s E ring, which is formed from the moon’s icy plume.

and magnesium. Collisional grinding of those minerals—the rough-and-tumble shattering of rock to make ever smaller pieces—might conceivably create silica nanoparticles. Yet such particles would come in a wide range of sizes, not the very narrow range Cassini observed. Only one other natural explanation remained: the nanoparticles could have crystallized from a supersaturated, silica-rich solution of hot, alkaline water flowing through rock—that is, from hydrothermal vents of exactly the kind found at Lost City on Earth.

A HABITABLE OCEAN?

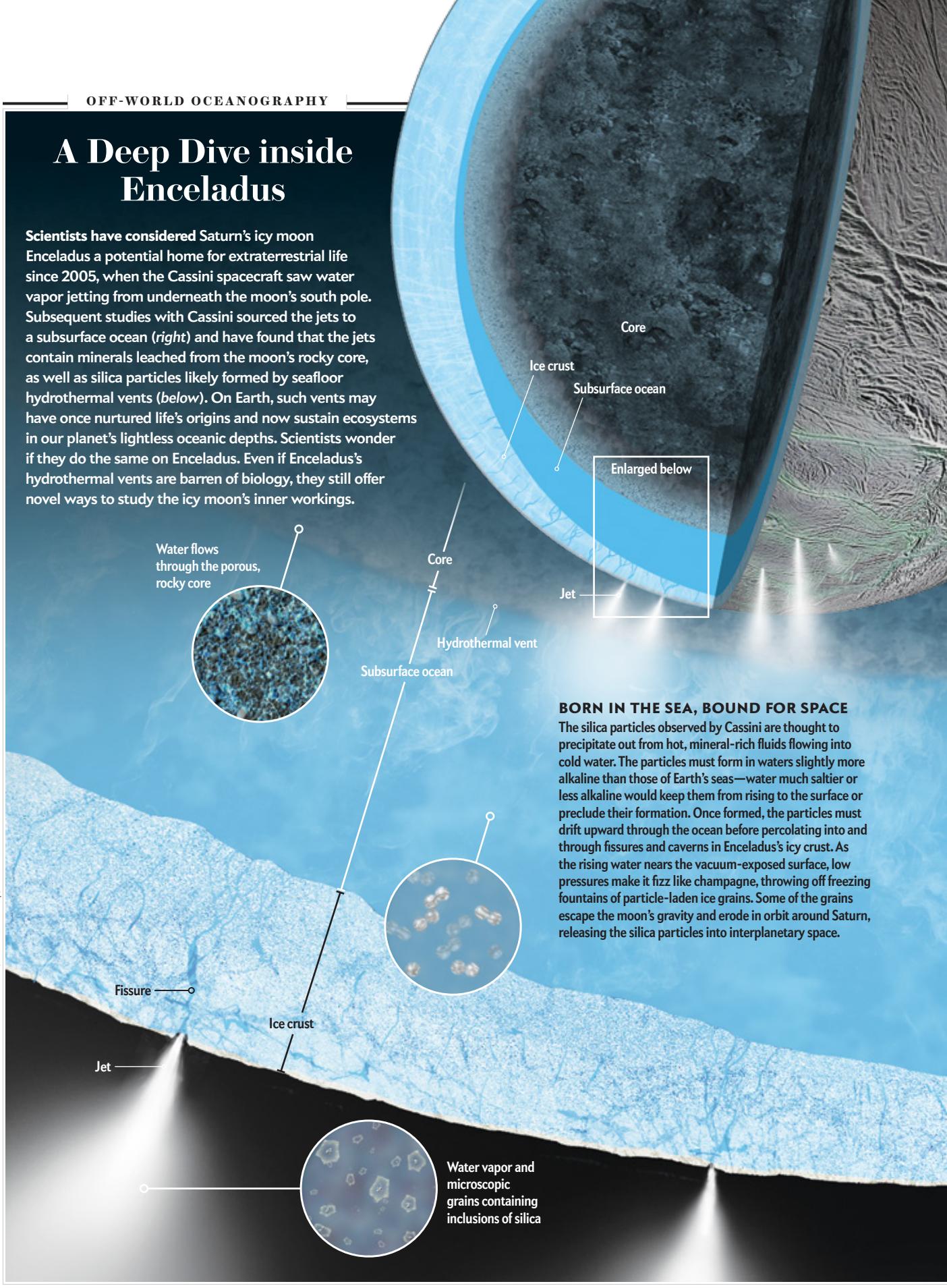
AT LOST CITY, and presumably on the seafloor of Enceladus, hot water absorbs silica as it flows up through silicate rocks. As the water vents out into the surrounding sea and cools, its capacity to carry absorbed minerals diminishes, and silica nanoparticles form. At this stage, other molecules could glom onto the nanoparticles, making them larger and heavier and thus causing them to eventually precipitate to the bottom—unless, that is, the water were alkaline and not too salty. This relation between the size and longevity of nanoparticles and the temperature and chemistry of their aqueous birthplaces offers researchers an unprecedented window into the environmental conditions of Enceladus’s ocean.

Following on Cassini’s initial detection of the nanoparticles, a team led by Yasuhito Sekine of the University of Tokyo conducted laboratory experiments to confirm how the nanoparticles formed and to reveal the conditions deep within Enceladus. The scientists found that water at or above 90 degrees Celsius with alkalinity above and salinity slightly below the value of Earth’s sea is ideal for creating small, long-lived silica nanoparticles. According to their experiments, the alkalinity of Enceladus’s ocean must be between that of terrestrial seawater and ammonia-based household cleaning products. If it were more alkaline than aqueous ammonia, the water’s high silica solubility would not allow nanoparticles to form. If the water were less alkaline than seawater on Earth, it would have to be inconceivably hot to dissolve sufficient amounts of silicon dioxide to form silica nanoparticles.

A Deep Dive inside Enceladus

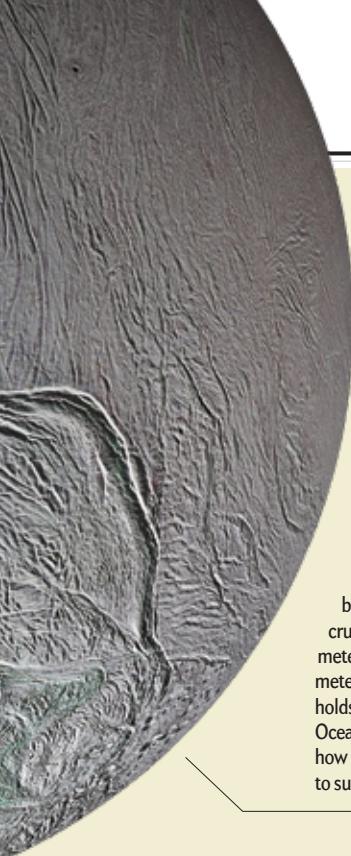
Scientists have considered Saturn's icy moon Enceladus a potential home for extraterrestrial life since 2005, when the Cassini spacecraft saw water vapor jetting from underneath the moon's south pole. Subsequent studies with Cassini sourced the jets to a subsurface ocean (right) and have found that the jets contain minerals leached from the moon's rocky core, as well as silica particles likely formed by seafloor hydrothermal vents (below). On Earth, such vents may have once nurtured life's origins and now sustain ecosystems in our planet's lightless oceanic depths. Scientists wonder if they do the same on Enceladus. Even if Enceladus's hydrothermal vents are barren of biology, they still offer novel ways to study the icy moon's inner workings.

SOURCE: NASA/JPL-CALTECH/SPACE SCIENCE INSTITUTE/LUNAR AND PLANETARY INSTITUTE (Enceladus surface map)



BORN IN THE SEA, BOUND FOR SPACE

The silica particles observed by Cassini are thought to precipitate out from hot, mineral-rich fluids flowing into cold water. The particles must form in waters slightly more alkaline than those of Earth's seas—water much saltier or less alkaline would keep them from rising to the surface or preclude their formation. Once formed, the particles must drift upward through the ocean before percolating into and through fissures and caverns in Enceladus's icy crust. As the rising water nears the vacuum-exposed surface, low pressures make it fizz like champagne, throwing off freezing fountains of particle-laden ice grains. Some of the grains escape the moon's gravity and erode in orbit around Saturn, releasing the silica particles into interplanetary space.



MAPPING A MOON'S INTERIOR

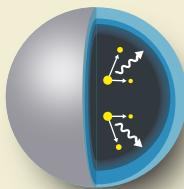
Based on its proposed hydrothermal activity, as well as observations of Enceladus's gravitational field, rotation, surface features and plume composition, researchers now possess a remarkably detailed view of the moon's interior. The subsurface ocean is global in extent, sandwiched between a rocky, porous core and a frozen crust that ranges in thickness from 35 kilometers at the equator to less than five kilometers at the south pole. In total, it probably holds a tenth as much water as the Indian Ocean. Scientists do not yet know exactly how the tiny moon generates enough heat to sustain this large ocean.

HOW LONG CAN THE OCEAN LAST?

For life as we know it to exist on Enceladus, its ocean must be long-lived and persistent. If instead the ocean is transient, only lasting a few tens of millions of years or cycling through frozen and thawed states, then the moon is likely lifeless. The ocean's longevity is intimately tied to the same mysterious heat supply that powers the moon's hydrothermal activity. Scientists have identified three possible heat sources for the moon, each with different implications for the ocean's longevity.

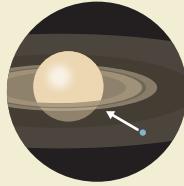
Radioactive Decay

Radioactive isotopes release heat as they decay. Enceladus is thought to be comparable to Earth in isotope abundance, but the moon is so small that it would rapidly deplete and lose this radiogenic heat, causing its ocean to freeze long ago.



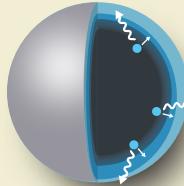
Tidal Friction

The gravitational pull of Saturn and nearby moons raises tides within Enceladus that flex its interior, creating heat from friction that could in principle warm the moon for billions of years. Saturn's influence, however, could also alter the moon's orbit in ways that reduce the amount of internal heating, leaving Enceladus cold in only a million years or less.



Serpentization

"Serpentization" reactions between water and rock can release heat, but as with radioactive decay, this heat tapers off over time as rock is transformed by the chemical reactions. Yet tidal friction could boost and extend serpentization by regularly exposing fresh rocks to water percolating through the moon's porous core.



Altogether, Hsu's, Postberg's and Sekine's respective work raises the possibility that the rich ecosystems of Lost City and other terrestrial hydrothermal vents could conceivably survive and thrive if relocated to the depths of Enceladus. In other words, the ocean of this distant icy moon looks like it could be habitable.

Of course, it could be that Enceladus is currently inhospitable for life and that the silica nanoparticles detected by Cassini are simply relics of ancient hydrothermal activity that ceased long ago. But the work of Sekine and other collaborators suggests this is not the case. In lab experiments and numerical models, freshly formed silica particles average about four nanometers wide, only growing larger over time spans of at least a few months and, at most, a few years. The CDA data show that the typical nanoparticle from Enceladus is between four and 16 nanometers wide, with none wider than 20. Hence, the nanoparticles collected by Cassini must have been created only a short time before being measured. Otherwise, they would have been larger than observed. This is as close as we can come to proving that, as you read this, hydrothermal vents are churning away on the seafloor of Enceladus.

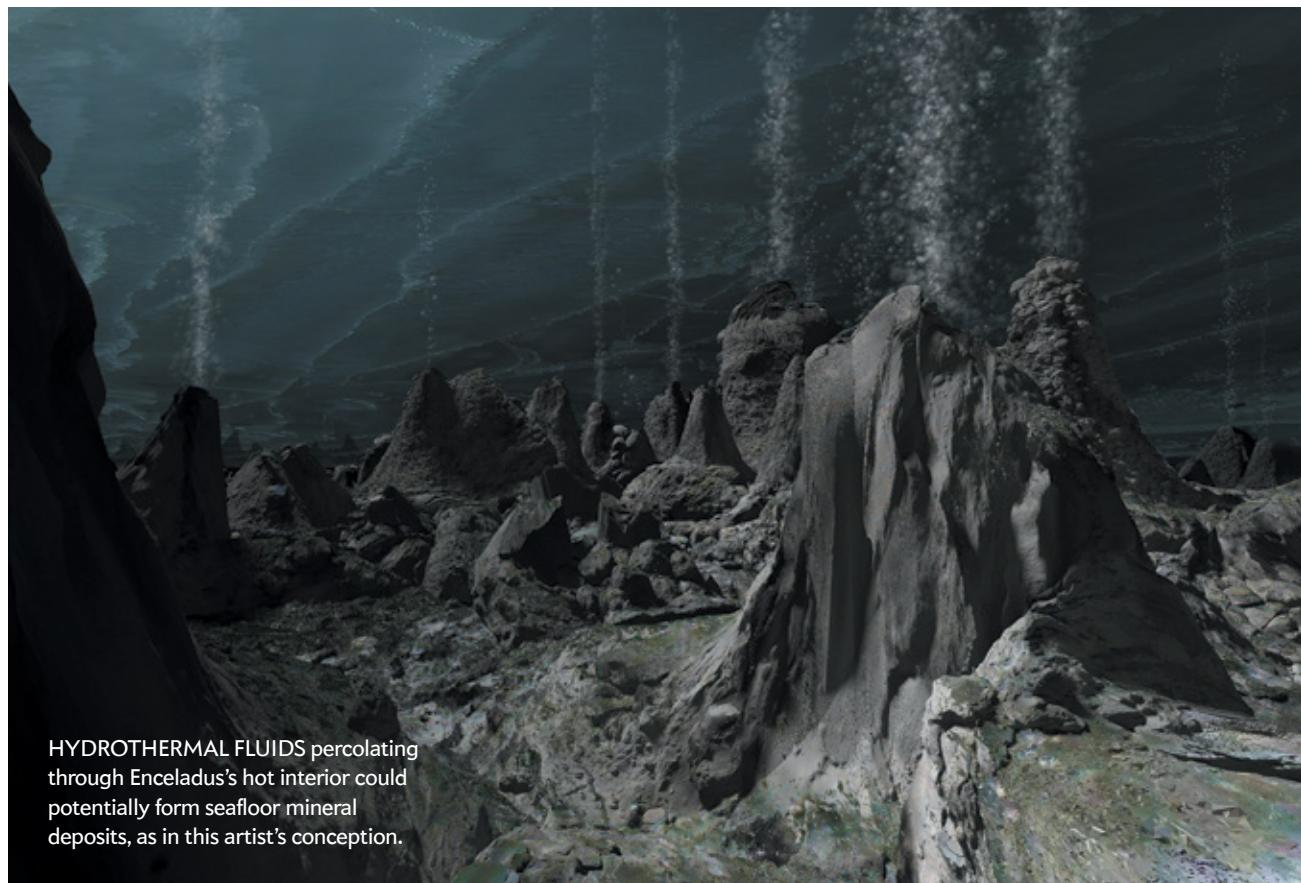
FROM SEAFLOOR TO DEEP SPACE

BASED ON THE MECHANICS we have uncovered, we can now trace a typical nanoparticle's journey from the bottom of Enceladus's buried sea out to the wider solar system. After forming at the cooling edges of hot, silica-rich fluids gushing into the cold surrounding ocean, a nanoparticle will spend as much as a few years drifting up through about 60 kilometers of open water.

When it reaches the top of the ocean, the nanoparticle ascends into water-filled fractures that crisscross through the few-kilometer-thick overlying frozen crust of the south polar terrain. Because the seawater is denser than the surrounding ice, its progress upward should halt less than a kilometer underneath Enceladus's surface. But here the so-called champagne effect provides a further boost: as the water, which contains dissolved carbon dioxide, rises, and the pressure on it decreases, it becomes fizzy with carbon dioxide bubbles. The bubbles help to lift the seawater within perhaps 100 meters of Enceladus's surface.

There, we suspect, it pools in ice caves. In such close proximity to the harsh vacuum of space, bursting carbon dioxide bubbles and low pressures make the pools effervesce, throwing off clouds of mist and water vapor. The droplets of mist quickly freeze into micron-size ice grains, which incorporate the silica nanoparticles like raisins in a bun. The vapor rises up through channels in the brittle and dry near-surface ice, as if through a chimney. Some of the vapor freezes on the walls of ice, releasing latent heat that we see as the infrared glow of Enceladus's surface tiger stripes. The vapor that does not freeze carries the nanoparticle-laden grains up to the surface, hurling them into space as icy fountains.

Most of the grains in the plume fall back to the surface as snow, but those with the highest speeds escape Enceladus to accumulate in the E ring. In the E ring, ionized gas erodes the ice grains and frees the embedded nanoparticles. The liberated nanoparticles then accumulate an electric charge from the ionized gas and free electrons and become the playthings of Saturn's immense electromagnetic fields. Finally, boosted by solar winds, some of the nanoparticles reach velocities up to a million kilometers per hour—about 1 percent of light speed—and zip off into the solar system. A small fraction of the escapees may even reach interstellar space, to surf the voids between the stars.



HYDROTHERMAL FLUIDS percolating through Enceladus's hot interior could potentially form seafloor mineral deposits, as in this artist's conception.

HOT TOPICS

AS ELABORATE, BEAUTIFUL and, we believe, true as this narrative is, it does not address what has become the central conundrum of Enceladus: What is the source of the internal heat required to maintain its dynamic ocean? That heat, which is essential for liquid water and life, obviously cannot come from sunlight. The sun's rays are about 99 percent weaker at Enceladus than in Earth's vicinity, giving the icy moon a surface temperature about that of liquid nitrogen.

About half of Earth's internal warmth comes from the slow decay of radioactive isotopes of uranium, thorium and potassium. This radiogenic heating has sustained temperatures exceeding several thousands of degrees C in Earth's interior for billions of years. Although Enceladus probably contains comparable concentrations of radiogenic elements, at only 500 kilometers wide, the diminutive moon loses its internal heat much more efficiently than Earth does. In the absence of an additional heat source, Enceladus's interior should be frozen solid. The moon's small size and weak gravity also make its internal dynamics very different from bulky planets like Earth: lower pressures and more moderate temperatures within Enceladus limit the compaction and consolidation of material in its core, allowing water to circulate down through porous rock to create hydrothermal processes in the moon's very center. Contrast this with Earth, where the rapid subterranean increases in pressure and temperature limit water circulation to the top few kilometers of crust.

One might expect the flushing of Enceladus's core to hasten

its cooling, sweeping away any radiogenic heat and precluding the high temperatures required to make silica nanoparticles. Yet there is another possible energy source beyond standard radiogenic heating that could explain the moon's present-day hydrothermal activity: tidal heating.

Similar to how Earth's ocean tides arise from our moon and the sun pulling on our planet, tidal heating occurs when a planet's or moon's interior periodically flexes as it moves through a noncircular, eccentric orbit. The flexure from shifting gravitational forces creates friction in a planet's or moon's inner layers, which in turn creates heat. Tidal heating would be particularly powerful within the porous, water-suffused core of a world such as Enceladus. And indeed, data from Cassini clearly show that Saturn's tidal pull profoundly influences the tiny moon—the brightness of its erupted jets and therefore the amount of material ejected vary periodically as the moon whirls around the ringed planet. Evidently, the chimneylike cracks that serve as conduits for mist and water vapor through the ice are at turns squeezed together and pulled apart by tidal tugs that also generate significant amounts of heat.

THE TURNING OF THE TIDE

WHAT WE DO NOT KNOW is whether the ocean we observe today is a transient phenomenon persisting for only tens of millions of years or a sustained feature of the moon that has endured for hundreds of millions or even billions of years. The answer depends on how long the action of tides has heated up Enceladus's

interior; which in turn depends on how the moon influences Saturn, as well as its lunar neighbor Dione.

To understand these tidal interactions, we can consider the familiar system of our Earth and moon, which bears some similarities to that of Saturn and Enceladus. Our moon raises tides on Earth, and Enceladus does the same to Saturn. In Earth's ocean, these tidal flows gradually dissipate because of friction against coastlines and the seafloor—an effect that measurably slows Earth's rotation. One hundred years from now, the day will be two milliseconds longer than it currently is, and Earth will have sapped enough of lunar tidal energy to push the moon's orbit out by nearly four meters. Similarly, tidal friction in Saturn's interior infinitesimally affects the giant planet's rotation while increasing Enceladus's distance from Saturn and orbital eccentricity. Higher eccentricities translate into larger tidal effects—and thus more heating—within Enceladus. Early theoretical estimates suggested that Enceladus would raise only weak tidal friction within Saturn, leading to the moon's orbit losing its eccentricity and thus limiting the lifetime of any tidal-heated ocean to no more than one million years.

Recently Valéry Lainey of the Paris Observatory and his collaborators (including Tobie) performed detailed analyses of the motions of Saturn's large moons to place more accurate constraints on the magnitude of tidal friction in the giant planet's interior. They found that the tidal friction within Saturn is at least 10 times larger than predicted by previous models. If true, this larger figure would mean that Enceladus's orbital eccentricity is stable and long-lived, allowing strong tides that can sustain an ocean for at least tens of millions of years and potentially much, much longer. The longer Enceladus's ocean can persist, it would seem, the greater the likelihood of life's emergence and flourishing there.

BRAVE NEW UNDERWORLDS

IN THE MEANTIME, there is a second possible heat source to consider beyond tidal heating. When water percolates through silicate rock, it can hydrate and change the crystalline structure of certain minerals, releasing substantial amounts of heat in a process called serpentinization. Bolstered by the ready circulation of water through the moon's porous, silicate-rich rocky core, serpentinization could generate several gigawatts of power and be a crucial part of Enceladus's internal heat budget. As long as fresh, unaltered minerals are in contact with circulating water, this heat supply will persist. But as the rock becomes fully serpentinized over millions of years, it will cease producing heat and should cool down in the absence of other influences, such as tidal friction. So it seems that serpentinization alone can hardly sustain a global ocean long enough to allow prebiotic chemistry to evolve.

Even so, serpentinization could still contribute to possible biospheres within Enceladus's depths. On Earth, scientists have observed serpentinization processes powering the hydrothermal vents at Lost City and other undersea sites. Besides making heat, these reactions also produce hydrogen, methane and other organic compounds that sustain the microbes that form the base of the food chain for their isolated, sun-starved ecosystems. Studying such organisms, some researchers have wondered whether life really needs the sun at all.

In the late 1980s Michael Russell, then at the University of Strathclyde in Scotland, and his collaborators hypothesized that alkaline hydrothermal vents might have been the birthplace of

the first living organisms on the early Earth. Although none were yet known on Earth, Russell argued that such sites would offer a relatively benign yet energy-rich environment in which prebiotic chemistry could brew to form the precursors of modern membranes, metabolisms and self-replicating molecules. Few people took the idea seriously enough to discuss or debate it outside of rarified academic circles.

The discovery of Lost City catalyzed new interest in Russell's hypothesis, catapulting it to the forefront of contemporary discussions of life's origins. Now the discovery of similar environments within Enceladus—and the potential for their existence in other icy moons such as Jupiter's Europa—is catalyzing another shift in how we think about the possibilities for life elsewhere in the solar system. Biology need not be confined to the warm, wet surfaces of sunlit rocky planets but could perhaps proliferate in a much wider range of environments, sustained in whole or in part by heat from radioisotopes, serpentinization or tidal forces. Enceladus and Europa may be proverbial tips of the iceberg—telltale hints that subsurface oceans also exist in Jupiter's moons Ganymede and Callisto, as well as Saturn's moons Titan and Mimas and even the dwarf planet Pluto. Researchers who, like us, are interested in life beyond Earth are only beginning to grapple with these speculative possibilities and their implications, but it appears increasingly likely that until now, we have drastically underestimated the universe's biological fecundity.

For the time being, we must remain in the dark about whether the interiors of icy moons really do supply all the necessary ingredients for extraterrestrial habitability. The duration and intensity of hydrothermal activity within Enceladus remain an open issue, and discussion of possible hydrothermal activity inside Europa is scarcely more than speculation. Both NASA and its counterpart the European Space Agency are eagerly pursuing answers to these questions and are planning missions to Jupiter's icy moons that could seek Enceladus-style plumes in the late 2020s or early 2030s. Cassini will continue to investigate Enceladus until the end of its mission in 2017, when it crashes into Saturn's depths to preclude any possibility of contaminating Enceladus or another icy moon with earthly biology. Eventually a new generation of spacecraft could be sent there to undertake in situ investigations, landing on the moon and even gathering samples for return to Earth. At present, such missions exist only in the hopes and dreams of astrobiologists—but perhaps not for long. ■

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HEALTH



THE RIGHT PILL FOR YOU

Now personalized genetic medicine offers tests to avoid dangerous drug reactions—yet doctors are reluctant to use them

By Dina Fine Maron

IN BRIEF

About half of all medical patients get a drug, in any given year, that could interact with their genes and cause serious side effects.

Inexpensive gene tests, which are as yet only available in a few hospitals, could avoid these life-threatening problems.

Yet lack of insurance reimbursement and doctors' confusion over when and how to alter drug prescriptions hold back widespread use of the new tests.

Dina Fine Maron is an associate editor at *Scientific American*.



K

OREI PARKER IS A BOISTEROUS SEVEN-YEAR-OLD WITH AN INFECTIOUS SMILE who improvises her own songs and loves to share them out loud. On an April day two years ago in Memphis, Tenn., where she lives, Korei came home from school with strange bruises. She had bumped into some things, she said—maybe a desk—but not hard enough to cause deep marks. Her mother, Rhonda, called their pediatrician and set up an appointment for later that week. But the next morning Korei woke up with new splotches across her arm and forehead. And when Korei brushed her teeth, her gums started to bleed.

Mother and daughter rushed to nearby St. Jude Children's Research Hospital. Doctors there figured out Korei was not producing enough new blood cells, which causes uncontrolled bleeding, bruising and infections. The illness is called severe acquired aplastic anemia.

The girl was quickly put on several drugs to boost her blood cells and fight infections. St. Jude doctors also did something unusual: they tested Korei for some 230 genes that affect which drugs—and what doses—would work best in her body. Certain gene variants can trigger the body to break down medications very quickly. In such cases, even high drug doses may fail.

Because of her particular genetics, the tests showed, Korei broke down voriconazole—a drug doctors had initially prescribed to stave off fungal infections—to fast. "She took adult dosages, and it didn't seem to do anything for her," Rhonda says. Her daughter had not contracted a dangerous fungus yet, but she was vulnerable, and her body would not be able to fight back. So physicians switched to another drug that interacts with bodily enzymes made by different genes. Korei's body processed that drug normally, and she remained infection-free.

Tailoring treatments to genetic makeup is part of the futuristic vision of personalized medicine, where all care is custom-fit to an individual's DNA. Remarkably, part of that vision—genetic drug matching, called pharmacogenomics—is already here. Korei Parker benefited from it. Although total human genome sequencing costs \$1,000, getting drug-gene results on a few hundred genes at St. Jude costs about half that much for

each patient. "The era of precision medicine is upon us," says Dan Roden, assistant vice chancellor for personalized medicine at Vanderbilt University Medical Center. "The low-hanging fruit here is pharmacogenomics."

Unfortunately, this fruit is being plucked by only a handful of hospitals. Lack of insurance coverage for the tests, along with confusion among doctors about what to do with the genetic data, is preventing the exams from being widely used.

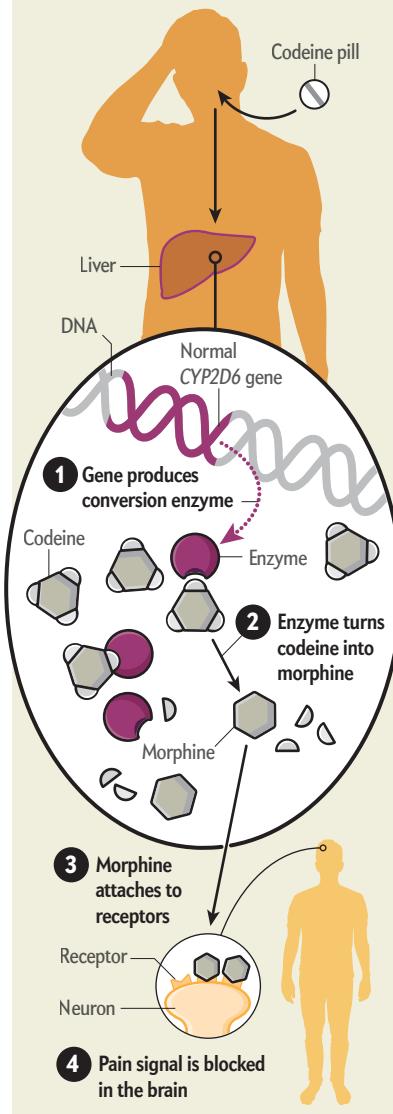
The sad result, advocates say, is that people are getting sick needlessly. Between 5 and 30 percent of the global population is estimated to have the same troublesome gene variant as Korei, for example, and it affects how well people respond to multiple medications, not just voriconazole. Roughly 50 percent of hospital patients get a drug in any one-year period that could cause serious side effects because of that person's genetic makeup, according to analyses from St. Jude and Vanderbilt. One study at Vanderbilt, which examined only six drugs, estimated that drug-gene tests could eliminate some 400 adverse events in a patient population of 52,942. If tests were performed for more than six drugs across the U.S. population, that number of avoided ailments would likely climb into the hundreds of thousands.

SHOTS IN THE DARK

DOCTORS ARE NOT ACCUSTOMED to making medication choices using genetics. What they have done, for decades, is to look at easily observed factors such as a patient's age and weight and kid-

A Just Right

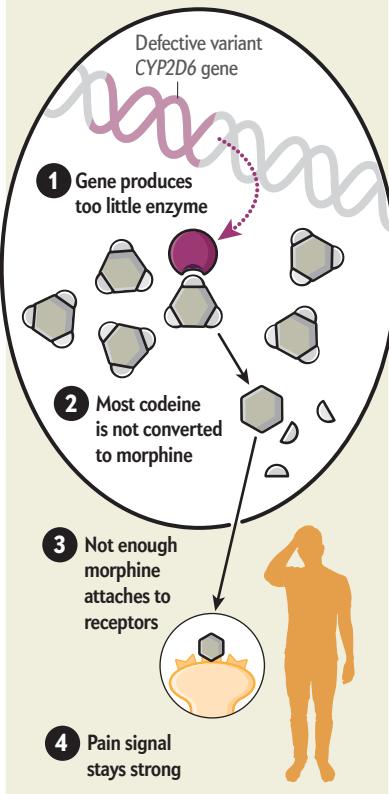
A gene called *CYP2D6* produces the enzyme that helps to convert codeine into morphine. When a patient has two normal copies of the gene, he or she produces enough enzyme to yield the right amount of morphine. It attaches to cell receptors in the brain and spinal cord, blocking pain signals from getting through.

**Preventing Pain**

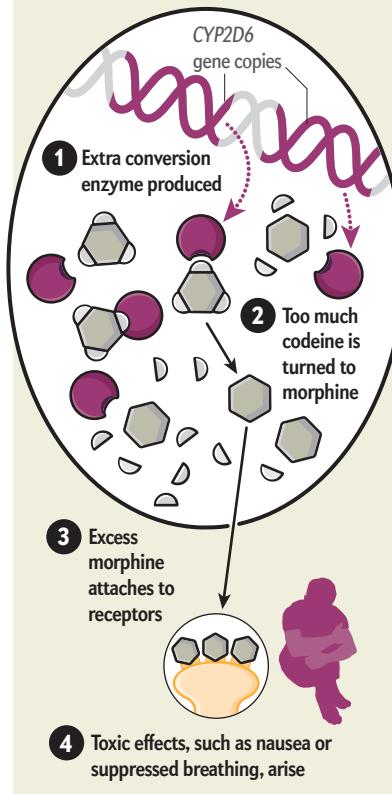
Genetic differences mean that codeine, a common painkiller, does not work the same way in everyone. An enzyme in the liver usually transforms codeine into morphine, the true pain-blunting molecule **A**. But some people have a defective version of the enzyme **B** or do not make it at all; others produce too much of the substance **C**. DNA tests can reveal who has what, so that physicians can adjust the drug dose to fit the patient.

B Too Little

Up to 10 percent of the population have an underperforming form of the *CYP2D6* gene or are missing it all together. They do not make enough of the codeine-conversion enzyme.

**C Too Much**

Up to 2 percent of the population have extra copies of the *CYP2D6* gene, overproducing the enzyme and making too much morphine from a codeine dose.



ney or liver functions. They have also considered what other medications a patient is taking and any personal preferences.

If clinicians would consider genetics, here is what they could learn about prescribing the common painkiller codeine. Typically the body produces an enzyme called *CYP2D6* that breaks down the drug into its active ingredient, morphine, which provides pain relief. Yet as many as 10 percent of patients have genetic variants that produce too little of the enzyme, so almost no codeine gets turned into morphine. These

people get little or no help for their pain. About 2 percent of the population has the reverse problem. They have too many copies of the gene that produces the enzyme, leading to overproduction. For them, a little codeine can quickly turn into too much morphine, which can lead to a fatal overdose.

These types of drug-gene interactions explain some long-standing medical mysteries. As early as 510 B.C. Greek mathematician Pythagoras (of geometry-class fame) found that when some people ate a particular type of bean they would get hemo-

lytic anemia, a potentially deadly condition in which red blood cells are destroyed and removed from the bloodstream. Some 2,500 years later researchers discovered why that reaction occurred: these people inherit genetic variants that lead to a deficiency in the production of an enzyme called glucose-6-phosphate dehydrogenase (G6PD). That substance normally prevents red blood cell destruction. That very same genetic variant—which can be spotted with today's gene tests—also predisposes patients to hemolytic anemia if they take several drugs now on the market, including rasburicase, a medication often given to patients with leukemia.

Many such drug-gene interactions—both severe and subtle—could be avoided by taking different doses of the drugs or turning to substitutes. Researchers concluded in October 2015 in *Nature* that there are 80 medications—affected by about two dozen genes—with known alternative treatments.

Some of the major recent research milestones about drugs and genes have been reached at St. Jude by Mary Relling, chair of the pharmaceutical sciences department. St. Jude sees a lot of pediatric cancer patients, and because many potential problem drugs are chemotherapy medications, the hospital was worried these children could be hurt by genetic interactions. Relling and her colleagues conducted years of drug-gene tests on a small scale. Then, in May 2011, she spearheaded the effort to start testing all new St. Jude patients.

The hospital also has a major advantage over others: it does not have to worry about insurance companies paying the institution back for these gene tests or denying the claims and making patients themselves pay. Patient care is paid for primarily by donations and grants. Thanks to that financial certainty, whenever a new patient starts care, St. Jude tests a blood sample for more than 200 genes.

By March of this year the hospital had data in almost 3,000 patients' electronic medical records corresponding to seven genes and 23 drugs that are well understood and affect its patients. One record belongs to Eden Brewer, a five-year-old girl who was diagnosed with acute lymphoblastic leukemia at the hospital last year. Fortunately, her gene test results did not reveal any mutations that would require the doctors to change their treatment plan. But they did reveal she might have trouble with other drugs later on in life. One is called simvastatin, used to manage high cholesterol. Eden, it turns out, has a variant form of a gene, known as *SLCO1B1*, that would keep her body from effectively processing the drug. For reasons that are not yet fully understood, that

problem sometimes leads to life-threatening muscle damage. Simvastatin is a frequently prescribed drug, but Eden needs to stay away from it.

"It's exciting to have that kind of knowledge," says her mother, Nicole. "We have this new tool in our belt not just for while we're here at St. Jude but for her whole life—forever." If a doctor at St. Jude ever tries to prescribe this medication, a warning box will pop up on her electronic record.

FAIR WARNINGS

VANDERBILT UNIVERSITY Medical Center is one of the few other institutions in the country that is using pharmacogenomics to help its patients. Roden, the personalized medicine head, likes to tell the story of the center's first patient to benefit back in 2010. The 68-year-old woman had been coming to Vanderbilt for care after a heart transplant, and her doctor had inserted a stent to prop open one of her blood vessels. Then he tried to prescribe clopidogrel, a drug typically used to prevent in-stent blood clots. When he typed the medication name into her electronic medical record, however, an alert popped onto the screen stating the patient's gene tests indicated she would metabolize the drug poorly. The alert was part of Vanderbilt's then new effort to experiment with pharmacogenomics. It suggested another drug, prasugrel, which would not run afoul of these genes.

Six years later Vanderbilt continues to focus on heart patients because it has been able to document several genetic effects on cardiac medications. One hospital analysis, which looked at more than 9,500 of its patients, found that 91 percent had at least one gene version that would prompt doctors to recommend a change in dose or medication. A subset of those patients—roughly 5 percent—had two copies of genes that would boost their chances of conditions such as stroke or heart attack from a clot if they took those

medications at standard doses.

Vanderbilt, like St. Jude, has mostly shouldered the costs of these tests because of the insurance problem. The insurance companies say they will cover only some tests because not all have been definitively shown to improve clinical outcomes. "Coverage does vary for these tests as a result of limited clinical evidence around their effectiveness for patients," says Clare Krusing, a spokesperson for America's Health Insurance Plans, the national trade association for the health insurance industry.

There are signs that this skepticism is beginning to soften. Vanderbilt officials say that in the past few years reimbursement policies from some insurers have evolved, and companies



1



2

GENE-TESTING RESULTS helped doctors decide what medication to give Korei Parker (1) at St. Jude Children's Research Hospital. Eden Brewer, a patient at St. Jude, and her doctor, Raul Ribeiro, also took advantage of the tests (2).

have started to cover a small percentage of the costs. Other hospitals are taking note. Several years after Vanderbilt started offering tests, the University of Maryland Medical Center started offering them, too—though, like Vanderbilt, usually just to cardiovascular patients. That institution has used clinical research grants from the federal government to cover the testing costs for more than 600 patients. But Maryland hopes to change over to billing insurance companies soon, according to Amber Beitshees, one of the people heading up the Maryland effort.

Still, fewer than 10 hospitals around the country—including Maryland, Vanderbilt and St. Jude—are offering pharmacogenomic tests to certain patients. The other main obstacle to wider use, besides reimbursement, is the lack of a prescribing road map. Many doctors were educated in an era before such testing was available, so they do not even think to order them. And a lot of physicians would likely find they are not equipped to understand the results. “You need more than this raw information—you must build the informatics tools—decision-support systems,” Roden says. A busy doctor needs to be told the patient had genetic testing for certain variants and what the tests found and be given easy-to-understand guidance on what prescribing changes could be made, he notes.

St. Jude pharmacists work on alerting doctors about alternative medications. The hospital also has created fact sheets about the significance of particular genetic variants, and those sheets are given to patients with any test results.

The accuracy of these tests is another important issue. The U.S. Food and Drug Administration has taken steps to regulate genetic tests when they are offered directly to consumers. In 2013, for example, the FDA ordered the genetic-testing company 23andMe to stop offering its flagship Personal Genome Service kit. The agency maintained 23andMe failed to provide adequate evidence that the product provided accurate results. Since that version of the product went off the market, other offerings have moved to help fill that niche—with a particular focus on pharmacogenomics. Genetics company DNA4Life, for example, started offering a \$249 consumer DNA test designed to predict drug response. But last November the FDA sent the company a stern letter saying that it would either need to get marketing approval to continue being sold to consumers or convince the agency why it should be exempt. The FDA says it cannot comment on current discussions with the company. Generally, however, it maintains it is closely scrutinizing the tests because people could potentially get scammed or, worse, be given incorrect information that could hurt them.

What the FDA does not monitor are in-hospital tests such as the ones at St. Jude. In the 1970s, when regulations for hospital-developed tests were first crafted, such diagnostic probes were relatively simple, and it seemed adequate that tests were developed at federally certified laboratories. Now that complex ge-

netics are involved, and the tests are being used more often, the FDA has proposed stepping up its oversight. So far, however, it has no timeline for putting changes into action.

The situation, like insurance acceptance, may be slowly changing. At the moment, Relling is co-directing a research group—supported by funds from the National Institutes of Health—to carefully document any new drug-gene relations solidified with new research. With that information the scientists set standards about what genes should typically be tested and spell out what prescribing changes should be made based on test results. The standards they develop are intended to be given to other labs at other hospitals.

A doctor tried to prescribe clopidogrel, a drug used to prevent blood clots, to a woman. When he typed the medication into her electronic medical record, however, an alert said gene tests indicated she would metabolize the drug poorly.

As more of these tests are done and show patient benefits, experts hope the obstacles and resistance will shrink and eventually disappear. When more physicians learn about the problems with genetic interactions, Relling believes, they will be reluctant to prescribe drugs without the tests, and that will force more offerings from more institutions. “If you knew about this genetic information and you did not act on it,” she says, “you would not be practicing good medicine.” ■

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FROM OUR ARCHIVES

The Paradox of Precision Medicine. Jeneen Interlandi; *The Science of Health*, April 2016.

THE TRUTH BROKERS

Knowledge is forged in the laboratory, but before it reaches the people, it passes through mediators—the **government**, the **media** and the **scientific establishment**—each with its own agenda.

IN THIS SPECIAL REPORT,

we expose an insidious practice of manipulation of news in the U.S. government and elsewhere; a culture of silence that discourages scientists from speaking out about their work; and the disconnect between what scientists do and what the public hears about. — *THE EDITORS*

IN BRIEF

Federal agencies in the U.S. are using so-called close-hold embargoes and other methods to gain control of the journalists who cover them [see “How to Spin the Science News,” page 54].

A comparison of data on the institutions that produce the most high-quality scientific research with the studies that get the most press reveals a big gap [see “What Science Is Buzzworthy?” page 62].

Scientists have long faced institutional pressures that discourage them from speaking out directly to the public. That may be starting to change [see “The Plight of the Celebrity Scientist,” page 64].



Charles Seife is a professor of journalism at New York University and author of *Virtual Unreality: The New Era of Digital Deception* (Penguin Books, 2014).



POLICY

HOW TO SPIN

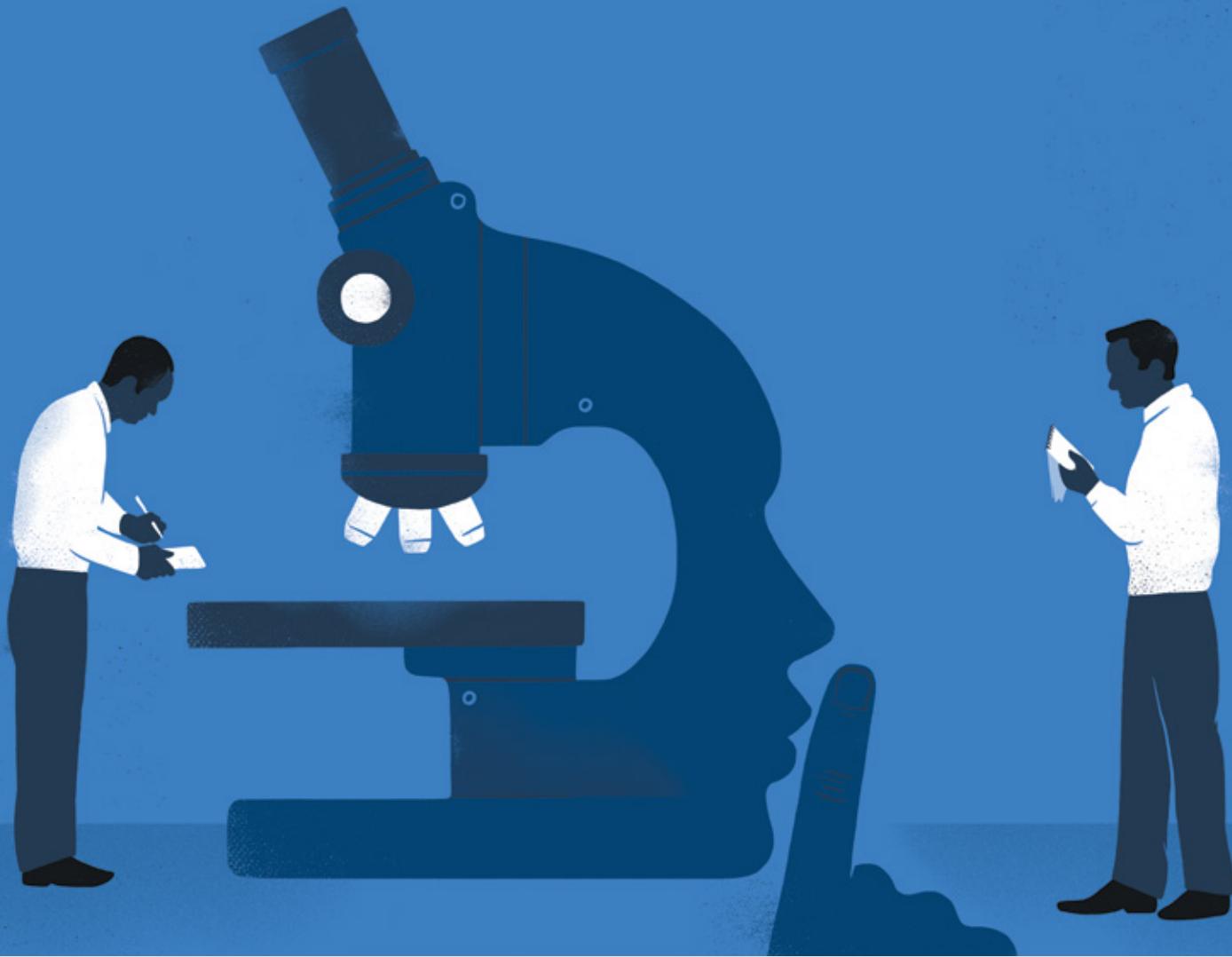
THE SCIENCE NEWS

The U.S. Food and Drug Administration has been arm-twisting journalists into relinquishing their reportorial independence, our investigation reveals. Other institutions are following suit

By Charles Seife

IT WAS A FAUSTIAN BARGAIN—and it certainly made editors at National Public Radio squirm.

The deal was this: NPR, along with a select group of media outlets, would get a briefing about an upcoming announcement by the U.S. Food and Drug Administration a day before anyone else. But in exchange for the scoop, NPR would have to abandon its reportorial independence. The FDA would dictate whom NPR's reporter could and couldn't interview.



"My editors are uncomfortable with the condition that we cannot seek reaction," NPR reporter Rob Stein wrote back to the government officials offering the deal. Stein asked for a little bit of leeway to do some independent reporting but was turned down flat. Take the deal or leave it.

NPR took the deal. "I'll be at the briefing," Stein wrote.

Later that day in April 2014, Stein—along with reporters from more than a dozen other top-tier media organizations, including CBS, NBC, CNN, the *Washington Post*, the *Wall Street Journal* and the *New York Times*—showed up at a federal building to get his reward. Every single journalist present had agreed not to ask any questions

of sources not approved by the government until given the go-ahead.

"I think embargoes that attempt to control sourcing are dangerous because they limit the role of the reporter whose job it is to do a full look at a subject," says *New York Times* former public editor Margaret Sullivan. "It's really inappropriate for a source to be telling a journalist whom he or she can and can't talk to." Ivan Oransky, distinguished writer in residence at New York University's Journalism Institute and founder of the Embargo Watch weblog, agrees: "I think it's deeply wrong."

This kind of deal offered by the FDA—known as a close-hold embargo—is an increasingly important tool used by scientific

and government agencies to control the behavior of the science press. Or so it seems. It is impossible to tell for sure because it is happening almost entirely behind the scenes. We only know about the FDA deal because of a wayward sentence inserted by an editor at the *New York Times*. But for that breach of secrecy, nobody outside the small clique of government officials and trusted reporters would have known that the journalists covering the agency had given up their right to do independent reporting.

Documents obtained by *Scientific American* through Freedom of Information Act requests now paint a disturbing picture of the tactics that are used to control the

science press. For example, the FDA assures the public that it is committed to transparency, but the documents show that, privately, the agency denies many reporters access—including ones from major outlets such as Fox News—and even deceives them with half-truths to handicap them in their pursuit of a story. At the same time, the FDA cultivates a coterie of journalists whom it keeps in line with threats. And the agency has made it a practice to demand total control over whom reporters can and can't talk to until after the news has broken, deaf to protests by journalistic associations and media ethicists and in violation of its own written policies.

By using close-hold embargoes and other methods, the FDA, like other sources of scientific information, are gaining control of journalists who are supposed to keep an eye on those institutions. The watchdogs are being turned into lapdogs. "Journalists have ceded the power to the scientific establishment," says Vincent Kiernan, a science journalist and dean at George Mason University. "I think it's interesting and somewhat inexplicable, knowing journalists in general as being people who don't like ceding power."

The press corps is primed for manipulation by a convention that goes back decades: the embargo. The embargo is a back-room deal between journalists and the people they cover—their sources. A source grants the journalist access on condition that he or she cannot publish before an agreed-on date and time.

A surprisingly large proportion of science and health stories are the product of embargoes. Most of the major science journals offer reporters advance copies of upcoming articles—and the contact information of the authors—in return for agreeing not to run with the story until the embargo expires. These embargoes set the weekly

rhythm of science coverage: On Monday afternoon, you may see a bunch of stories about the *Proceedings of the National Academy of Sciences USA* published almost simultaneously. Tuesday, it's the *Journal of the American Medical Association*. On Wednesday, it's *Nature* and the *New England Journal of Medicine*. Science stories appear on Thursday. Other institutions have also adopted the embargo system. Federal institutions, especially the ones science and health journalists report on, have as well. Embargoes are the reason that stories about the National Laboratories, the National Institutes of Health and other organizations often tend to break at the precisely same time.

Embargoes were first embraced by science reporters in the 1920s, in part because they take the pressure off. After all, when everybody agrees to publish their stories simultaneously, a reporter can spend extra time researching and writing a story without fear of being scooped. "[Embargoes] were created at the behest of journalists," says Kiernan, who has written a book, *Embargoed Science*, about scientific embargoes. "Scientists had to be convinced to go along." But scientific institutions soon realized that embargoes could be used to manipulate the timing and, to a lesser extent, the nature of press coverage. The result is a system whereby scientific institutions increasingly control the press corps. "They've gotten the upper hand in this relationship, and journalists have never taken it back," Kiernan says.

The embargo system is such an established institution in science journalism that few reporters complain or even think about its darker implications, at least until they themselves feel slighted. This January the California Institute of Technology was sitting on a great story: researchers there had evidence of a new giant planet—

Planet Nine—in the outer reaches of our solar system. The Caltech press office decided to give only a dozen reporters, including *Scientific American*'s Michael Lemonick, early access to the scientists and their study. When the news broke, the rest of the scientific journalism community was left scrambling. "Apart from the chosen 12, those working to news deadlines were denied the opportunity to speak to the researchers, obtain independent viewpoints or have time to properly digest the published research paper," complained BBC reporter Pallab Ghosh about Caltech's "inappropriate" favoritism in an open letter to the World Federation of Science Journalists.

When asked about why Caltech chose to release the news only to a select group of reporters, Farnaz Khadem, Caltech's head of communications, stated that she is committed to being "fair and transparent" about how and when Caltech shares news with journalists. She then refused to talk about the Planet Nine incident or embargoes or press strategy, and she would not grant access to anyone at Caltech who might talk about such matters. As a consequence, it is hard to know for certain why Caltech decided to share the news with only a select group of reporters. But it is not hard to guess why journalists such as Ghosh were excluded. "It wasn't that they were not good enough or not liked enough," Kiernan speculates. "There was a real effort here to control things, making sure that the elite of the elite covered this story and covered it in a certain way, which would then shape the coverage of all other journalists. It's very clearly a control effort."

Caltech is not the only institution that steers coverage by briefing a very small subset of reporters. (As I was writing this piece, I received a note from a U.S. Air Force press officer offering a sneak

By using close-hold embargoes and other methods, the FDA and other institutions gain control of journalists who are supposed to keep an eye on them.

preview of video footage being offered to “a select number of digital publications.”) For years the FDA has been cultivating a small group of journalists who are entrusted with advance notice of certain events while others are left out in the cold. But it was not the game of favorites that ignited a minor firestorm in the journalism community in January 2011—it was the introduction of the close-hold embargo.

Like a regular embargo, a close-hold embargo allows early access to information provided that attendees not publish before a set date and time. In this case, it was a sneak peek at rules about to be published regarding medical devices. But there was an additional condition: reporters were expressly forbidden from seeking outside comment. Journalists would have to give up any semblance of being able to do independent reporting on the matter before the embargo expired.

Even reporters who had been dealing with the FDA for years were incredulous. When one asked the agency’s press office if it really was forbidding communications with outside sources, Karen Riley, an official at the FDA, erased all doubt. “It goes without saying that the embargo means YOU CANNOT call

around and get comment ahead of the 1 P.M. embargo,” she said in an e-mail.

“Actually it does need some saying, since this is a new version of a journalistic embargo,” wrote Oransky in his Embargo Watch blog. Without the ability to contact independent sources, he continued, “journalists become stenographers.” Kiernan echoes the sentiment: “[When] you can’t verify the information, you can’t get comment on the information. You have to just keep it among this group of people that I told you about, and you can’t use it elsewhere. In that situation, the journalist is allowing his or her reporting hands to be tied in a way that they’re not going to be anything, ultimately, other than a stenographer.”

The Association of Health Care Journalists (AHCJ), of which I am a member, publicly objected to the close-hold embargo, noting that it “will be a serious obstacle to good journalism. Reporters who want to be competitive on a story will essentially have to agree to write only what the FDA wants to tell the world, without analysis or outside commentary.” Faced by this opposition, the agency quickly backtracked. After a meeting with AHCJ leaders, Meghan Scott, then the agency’s acting

associate commissioner for external affairs, wrote: “Prior to your inquiry, the FDA did not have a formal news embargo policy in place.” The FDA was now establishing new ground rules that “will better serve the media and the public.”

Initially published online in June 2011, the FDA’s new media policy officially killed the close-hold embargo: “A journalist may share embargoed material provided by the FDA with nonjournalists or third parties to obtain quotes or opinions prior to an embargo lift provided that the reporter secures agreement from the third party to uphold the embargo.” Due diligence would always be allowed, at least at the FDA.

Health and science journalists breathed a sigh of relief. The AHCJ expressed gratitude that the FDA had changed its tune, and Oransky’s Embargo Watch congratulated the agency for backing down: “For doing the right thing, the FDA has earned a spot on the Embargo Watch Honor Roll. Kudos.” And the FDA had cleared up the misunderstanding and affirmed that it was committed to “a culture of openness in its interaction with the news media and the public.”

In reality, there was no misunderstanding. The close-hold embargo had become part of the agency’s media strategy. It was here to stay—policy or no policy.

It is hard to tell when a close-hold embargo is afoot because, by its very nature, it is a secret that neither the reporters who have been given special access nor the scientific institution that sets up the deal wants to be revealed. The public hears about it only when a journalist chooses to reveal the information.

We have a few rare instances where journalists revealed that close-hold embargoes were being used by scientists and scientific institutions after 2011. In 2012 biologist Gilles-Eric Séralini and

his colleagues published a dubious—later retracted and then republished—paper purportedly linking genetically modified foods to cancer in rats. They gave reporters early access under a close-hold embargo, quite likely to hamstring the reporters' ability to explore gaping holes in the article, a situation science journalist Carl Zimmer described as “a rancid, corrupt way to report about science.” In 2014 the U.S. Chemical Safety and Hazard Investigation Board (also called the CSB) released a report to journalists under a close-hold embargo. When challenged, the then managing director of the CSB, Daniel Horowitz, told Oransky’s Embargo Watch that the close-hold embargo was used “on the theory that this would provide a more orderly process.” He then stated that the board was going to “drop the policy in its entirety for future reports.” Privately, however, a CSB public affairs specialist noted in an e-mail, “Frankly, I wish we did have more stenographers out there. Government agencies trying to control the information flow is an old story, but the other side of the story is that government agencies that do good work often have a difficult time getting their story told in an era of journalistic skepticism and partisan bickering and bureaucratic infighting.”

Also in 2014 the Harvard-Smithsonian Center for Astrophysics (CfA) used a close-hold embargo when it announced to a dozen reporters that researchers had discovered subtle signals of gravitational waves from the early universe. “You could only talk to other scientists who had seen the papers already; we didn’t want them shared unduly,” says Christine Pulliam, the media relations manager for CfA. Unfortunately, the list of approved scientists provided by CfA listed only theoreticians, not experimentalists—and only an experimentalist was likely to see the flaw that doomed the study.

(The team was seeing the signature of cosmic dust, not gravitational waves.) “I felt like a fool, in retrospect,” says Lemonick, who, as one of a dozen or so chosen journalists, covered the story for *Time* (at the time, he was not on the staff of *Scientific American*).

The FDA, too, quietly held close-hold embargoed briefings, even though its official media policy forbids it. Without a source willing to talk, it is impossible to tell for sure when or why FDA started violating its own rules. A document from January 2014, however, describes the FDA’s strategy for getting media coverage of the launch of a new public health ad campaign. It lays out a plan for the agency to host a “media briefing for select, top-tier reporters who will have a major influence on coverage and public opinion of the

campaigns.... Media who attend the briefing will be instructed that there is a strict, close-hold embargo that does not allow for contact with those outside of the FDA for comment on the campaign.”

Why? The document gives a glimpse: “Media coverage of the campaign is guaranteed; however, we want to ensure outlets provide quality coverage of the launch,” the document explains. “The media briefing will give us an opportunity to shape the news stories, conduct embargoed interviews with the major outlets ahead of the launch and give media outlets opportunities to prepare more in-depth coverage of the campaign launch.”

Ten reporters—from the *New York Times*, the *Washington Post*, *USA Today*, the Associated Press, Reuters, ABC, NBC, CNN and NPR—were invited to have their



stories shaped. The day after the briefing, on February 4, everybody—except for the *New York Times*—ran with stories about the ad campaign. Independent comment was notably missing. Only NPR, which went live hours after the others, and CNN, in an update to its story midday, managed to get any reaction from anyone outside of the FDA. CBS plunked down an out-of-context quotation from the director of the Centers for Disease Control and Prevention, probably in hopes that readers wouldn't notice that it was two months old. Nobody else seems to have tried to get anyone who could critique the ad campaign.

The result was a set of stories almost uniformly cleaving to the FDA's party line, without a hint of a question about whether the ad campaign would be as ineffective as many other such campaigns. Not one of the media outlets said anything about the close-hold embargo. From the agency's point of view, it was mission accomplished.

The FDA had a much harder task two months later. The agency was about to make public controversial new rules about electronic cigarettes. It was nearly impossible to keep the story from leaking out ahead of time; days before the new rules were going to be published in April 2014, rumors were flying. Reporters around the country could smell the story and began to e-mail the FDA's press office with questions about the e-cigarette rules. The agency flacks would have to use all the powers at their disposal to control the flow of information.

"I've heard a number of rumors that the FDA will be releasing its proposed e-cigarette regulations on Monday," Clara Ritger, then a reporter with the *National Journal* asked on Friday, April 18. "I wanted to see if I could confirm that? If that's not accurate, do you have a timeline?" Stephanie Yao, then an

FDA press officer, dodged the question: "The proposal is still in draft form and under review. As a matter of policy, the FDA does not share draft rules with outside groups while a rule is still under review."

The fencing match was on. "Thank you for following up with the statement," Ritger responded. "While I know the proposal is still in draft form and under review, for my planning purposes I wanted to find out when the proposed regulations will be coming out?"

"Have you subscribed to FDA press announcements?" Jenny Haliski, then another FDA press officer, wrote back on Monday. "The proposed rule itself will be published in the *Federal Register*."

"Thanks for sending! I signed up," Ritger responded. "The only other question I had was when the proposed regulations would come out, off the record, for planning purposes?"

Not even an offer of being off the record could get the agency to spill the beans. "The FDA can't speculate on the timing of the proposed rule," Haliski replied.

But this was a carefully crafted half-truth. There was no need to speculate. Haliski and others in the press office knew quite well not just that the rule was going to be published on Thursday, April 24, but also that there was going to be a close-hold embargoed briefing on Wednesday. It's just that Ritger and the *National Journal* weren't invited.

The invite list had been drafted days earlier, and, as usual, the briefing was limited to trusted journalists: the same outlets from the ad campaign briefing in February, with the addition of a few more, which included the *Wall Street Journal*, the *Boston Globe*, the *Los Angeles Times*, Bloomberg News, Politico and the *Congressional Quarterly*. At the very same moment that the agency was discussing the embargoed briefing with some of their chosen report-

ers, anyone outside that small circle, like Ritger, was being thrown off the trail. Not even Fox News was allowed in.

Some within the FDA press office wondered why Fox was excluded, unlike the other major networks. "BTW, we noticed that Fox still wasn't on the invite list," Raquel Ortiz, then an FDA press officer, told Haliski.

"I have no national Fox reporter who had contacted me on this topic," Haliski responded. "All reporters invited to the briefing needed to have covered tobacco regulatory issues before."

Ortiz realized that this wasn't an honest answer: "But they definitely cover FDA/CTP [Center for Tobacco Products] and tobacco stories—[a colleague has] seen them."

"We don't have a good contact for Fox," Haliski insisted, rather lamely. A contact would not have been hard to find had they bothered to look. And, as chance would have it, the contact found them. Early the next morning, with plenty of time before the briefing, Fox's senior national correspondent—John Roberts, one-time heir apparent to Dan Rather—contacted Haliski asking for access. "I'm aware that the FDA will likely come out with its deeming rule regarding e-cigarettes in the next week or so. I'd like to have a story ready to go for the day (holding to any embargo)," he wrote. "Can we make that happen?"

"Hi, John, Have you subscribed to FDA press announcements?" Access denied.

"I was particularly troubled by it because I was the medical correspondent for *CBS Evening News* for a couple of years, and I had a very good relationship with the FDA and everybody there," says Roberts, who found out he was excluded after the other correspondents' stories came out. "I was told by these folks that Fox news wasn't invited because of 'past experiences with Fox.'"

A little after noon on Wednesday, April 23, the briefing went on as scheduled. All the reporters present understood the terms, as announced: "As discussed, under this embargo you will not be able to reach out to third parties for comment on this announcement. We are providing you with a preview of the information with this understanding." But by 2:30 P.M., the close-hold embargo was already fraying at the edges. FDA officials apparently got wind that a reporter was trying to talk to a member of Congress about the new rules. Even though it was not clear that this was a breach of the embargo—the interview was scheduled for after the embargo expired, and the reporter presumably did not share any crucial information ahead of time—it was bending the close-hold rules, and the FDA was livid. Within half an hour, FDA's Jefferson had fired off an angry e-mail to the close-hold journalists.

"It has been brought to our attention that there has already been a break in the embargo.... Third-party outreach of any kind was and is not permitted for this announcement. Everyone who participated agreed to this," she wrote. "Moving forward, we will no longer consider embargoed briefings for news media if reporters are not willing to abide by the terms an embargo.... We take this matter very seriously, and as a consequence any individuals who violated the embargo will be excluded from future embargoed briefings with the agency." Violate the rules, even in spirit, and you'll be left out in the cold with the rest.

The denials flew in. "This is very frustrating as someone who has consistently played by the rules and has covered CTP/FDA for years to be lumped in with a group of reporters that cannot respect your requests not to reach out to third parties," insisted then AP reporter Michael Felberbaum.

"I have of course always advocated that you work more closely with reporters like myself who clearly understand and cover this area consistently instead of reporters who are just assigned to handle on a whim."

But despite the scare about a breach, the secrecy held. When the embargo expired and the early news stories went online, the FDA had little to complain about; the embargo had worked once again to shape coverage. Felberbaum's piece, for example, quoted Margaret Hamburg, then head of the FDA, and Mitch Zeller, the head of the agency's CTP, but nobody else. Even after he updated his piece later in the day to get some outside comments, there was little hint of how controversial the new rules were. Members of the tobacco industry were generally unhappy with increased federal regulation of their business, while anti-tobacco advocates tended to argue that the new regulations were far too weak and took way too long to promulgate. And there was no mention, in Felberbaum's article, at least, that the agency had tried to regulate e-cigarettes several years earlier but was slapped down with a stinging rebuke from the U.S. District Court for the District of Columbia. (When asked about his work for the AP, Felberbaum—who has since quit his job as a reporter to become an FDA press officer—said, "I'm not really sure whether I'm comfortable discussing that at this point.")

Some of the other outlets, like NPR, injected a little more nuance into their pieces, despite the restrictions, by doing additional reporting after the embargo expired. (In a statement, NPR said that agreeing to the FDA's conditions was not a violation of ethics guidelines and "in no way influenced which other voices or ideas were included in the coverage.") Still, even those pieces did not

stray far from the key messages that the agency wanted to get across. Again the FDA found little to complain about. Except for one little thing.

Of all the media outlets, the *New York Times* was the only one to mention the close-hold embargo: "FDA officials gave journalists an outline of the new rules on Wednesday but required that they not talk to industry or public health groups until after Thursday's formal release of the document." ("I felt like I wanted to be clear with readers," Sabrina Tavernise, the author of the story, later told Sullivan, the *New York Times'* public editor at the time. "Usually you would have reaction in a story like this, but in this case, there wasn't going to be any.")

The FDA was not pleased that the omertà had been broken. "I have to say while I generally reserve my editorial comments, I was a little surprised by the tone of your article and the swipe you took at the embargo in the paper—when after combing through the coverage no one else felt the need to do so in quite that way," the FDA's Jefferson upbraided Tavernise in an e-mail. "To be clear, this is me taking stuff personally when I know I shouldn't, but I thought we had a better working relationship than this.... I never expect totally positive coverage as our policies are controversial and complex, but at least more neutral and slightly less editorialized. Simply put, bummer. Off to deal with a pissed Fox News reporter."

Tavernise promptly apologized. "Geez, sorry about the embargo thing. Editors were asking why we didn't get to see it so I was asked to put a line in to explain," she wrote. (Tavernise declined to comment for this article; Celia Dugger, one of the *New York Times* editors who handled the piece, said via e-mail: "As to the decision to describe the conditions of the embargo in the story, Sabrina and

I talked it over and agreed it was best to include them.”)

The FDA was not pleased that the secret of the close-hold embargo was out, and the excluded press was confused and angry. “In this particular instance, it struck me as very strange,” says Fox’s Roberts. “It was a government agency picking and choosing who it was going to talk to on a matter of public policy, and then the fact that I had a longstanding relationship with the FDA that, with this new administration, didn’t seem to matter.”

Oransky complained again on Embargo Watch about the FDA’s attempts to turn journalists “into stenographers.” Sullivan asked a few pointed questions of Jefferson, who, in Sullivan’s words, insisted that the FDA’s intent was “not to be manipulative but to give reporters early access to a complicated news development” and noted, in passing, that Tavernise had not objected to the terms of the close-hold embargo. But the damage was short-lived. Very little came of the complaints; Sullivan said that she would “like to see the *Times* push back—hard—against such restrictions in every instance and be prepared to walk away from the story if need be,” but there is no evidence of any substantial pushback by anyone.

The two-tiered system of outsiders and insiders that undergirds the close-hold policy is also still enforced. Major press outlets such as *Scientific American* and Agence France-Presse have written to the FDA to complain about being excluded but have not received any satisfaction from the agency. Months after the e-cigarette affair and following a different FDA story about food labeling that insiders had early access to, *Time* magazine complained about its lack of access to a select-press-only phone call. “*Time* was not included ... (they weren’t even on my radar to be honest with you), but we handled all their queries” the day after

the call, then FDA press officer Jennifer Corbett Dooren wrote.

Absent any indications from the agency, it is anyone’s guess whether the close-hold embargo is still in use at the FDA and, if so, how frequently. Unfortunately, the FDA refused to answer any questions. Because I am suing the agency for access to documents about embargo practices at the FDA, the press office, in a statement that failed to answer any specific questions, said that news embargoes “allow reporters time to develop their articles on complex matters in an informed, accurate way” and that its use of embargoes conforms to relevant government guidelines and best practices. The press office referred all questions to the FDA’s Office of the Chief Counsel, which did not supply answers.

Since the *New York Times* slip, no journalist covering the agency has openly mentioned being subject to such restrictions. *Scientific American* made a significant effort to contact many of the reporters believed to have agreed to an FDA close-hold embargo—including the AP’s Felberbaum, the *Times’* Tavernise, NPR’s Stein, and other reporters from Reuters, *USA Today* and the *LA Times*. None could shed any light on the issue. Some explicitly refused to speak to *Scientific American*; some failed to return queries; two had no recollection of having ever agreed to a close-hold embargo, including Tom Burton, a Pulitzer Prize-winning *Wall Street Journal* reporter and the only one willing to answer questions. “I didn’t remember it at all, and [even] after you told me, I didn’t remember,” he said. As far as he knows, Burton added, such embargoes are rare.

No matter how rare it might be, there is documentary evidence of its happening multiple times, and each instance since 2011 is a violation of the FDA’s official media policy, which explicitly bans close-

hold embargoes. This policy still stands, just as it did before the last close-hold embargo. The smart money says that the agency’s unofficial policy still stands, too—and the favoritism and close-hold embargoes continue. It is apparently too sweet an arrangement for the FDA simply to walk away.

Despite the difficulty of measuring the use of close-hold embargoes, Oransky and Kiernan and other embargo observers agree that they—and other variations of the embargo used to tighten control over the press—appear to be on the rise. And they have been cropping up in other fields of journalism, such as business journalism as well. “More and more sources, including government sources but also corporate sources, are interested in controlling the message, and this is one of the ways they’re trying to do it,” says the *New York Times’* Sullivan. “I think it should be resisted.”

As much blame as government and other institutions bear for attempting to control the press through such means, the primary responsibility lies with the journalists themselves. Even a close-hold embargo wouldn’t constrain a reporter without the reporter’s consent; the reporter can simply wait until the embargo expires and speak to outside sources, albeit at the cost of filing the story a little bit later.

Says Oransky: “We as journalists need to look inward a little bit and think about why all of us feel we absolutely have to publish something at embargo [expiration] when we don’t think we have the whole story?” Alas, Kiernan says, there isn’t any movement within the journalism community to change things: “I don’t know that journalists in general have taken a step back, [looking] from the 50,000-foot view to understand how their work is controlled and shaped by the embargo system.” ■

2016

WHAT SCIENCE IS BUZZWORTHY?

Scientific journals publish tens of thousands of studies every year; the public hears about only a tiny fraction of them. Nothing wrong with that, in theory: most scientific research is extraordinarily specialized. But it is natural to wonder which studies make it across that gap—and how.

Do the biggest producers of peer-reviewed research get the most press? Do the media cover scientific subjects in rough proportion to the attention that scientists give them? To find out, we compared data from the Nature Index, which ranks institutions by research output, with numbers from Altmetric, a research firm that tracks media coverage.

—The Editors

WHO TOPPED PUBLISHING CHARTS ...

The 25 most prolific institutions in science in 2015, as ranked by the Nature Index.

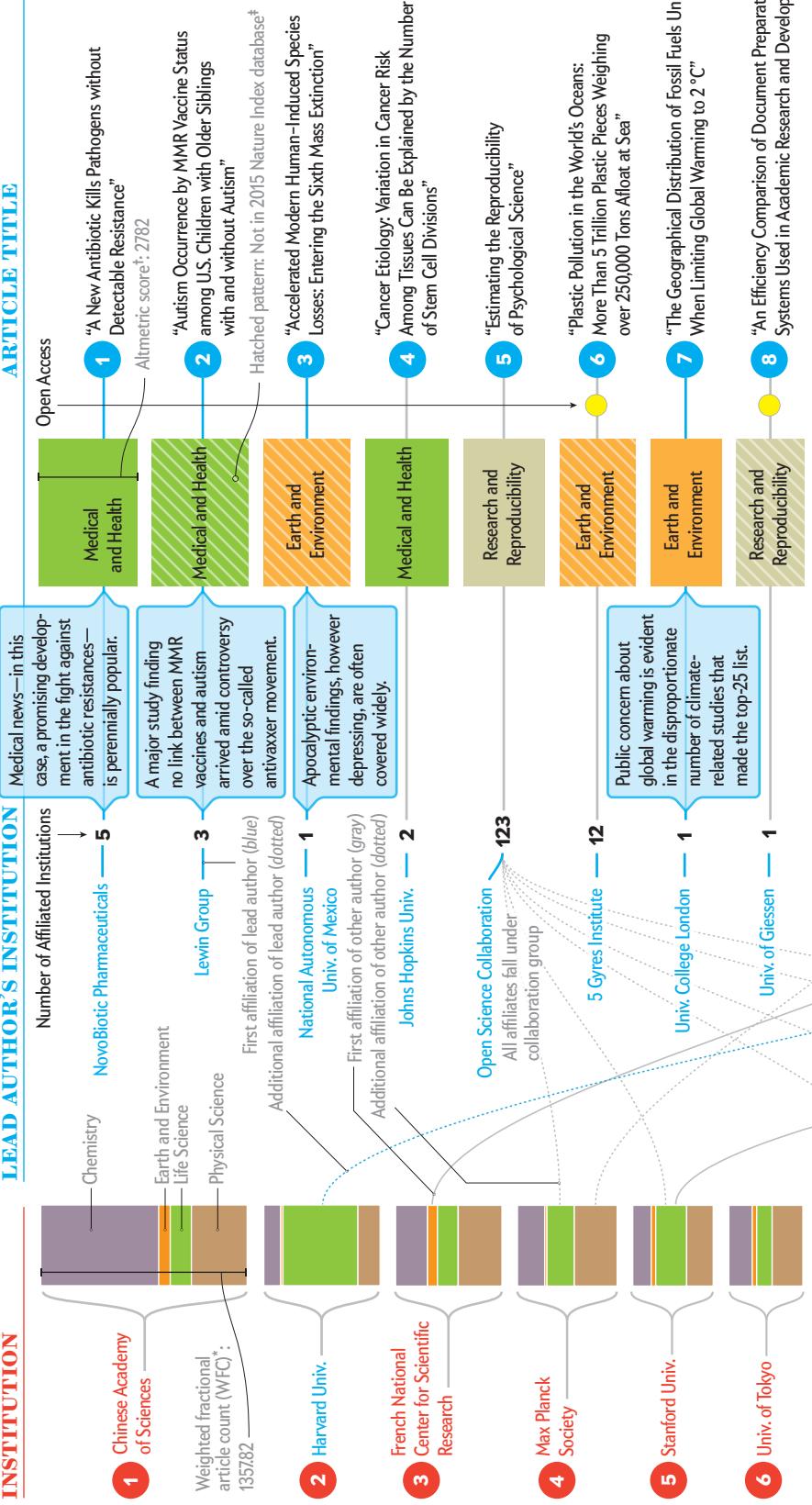
... AND WHO CREATED A BUZZ IN THE NEWS AND SOCIAL MEDIA

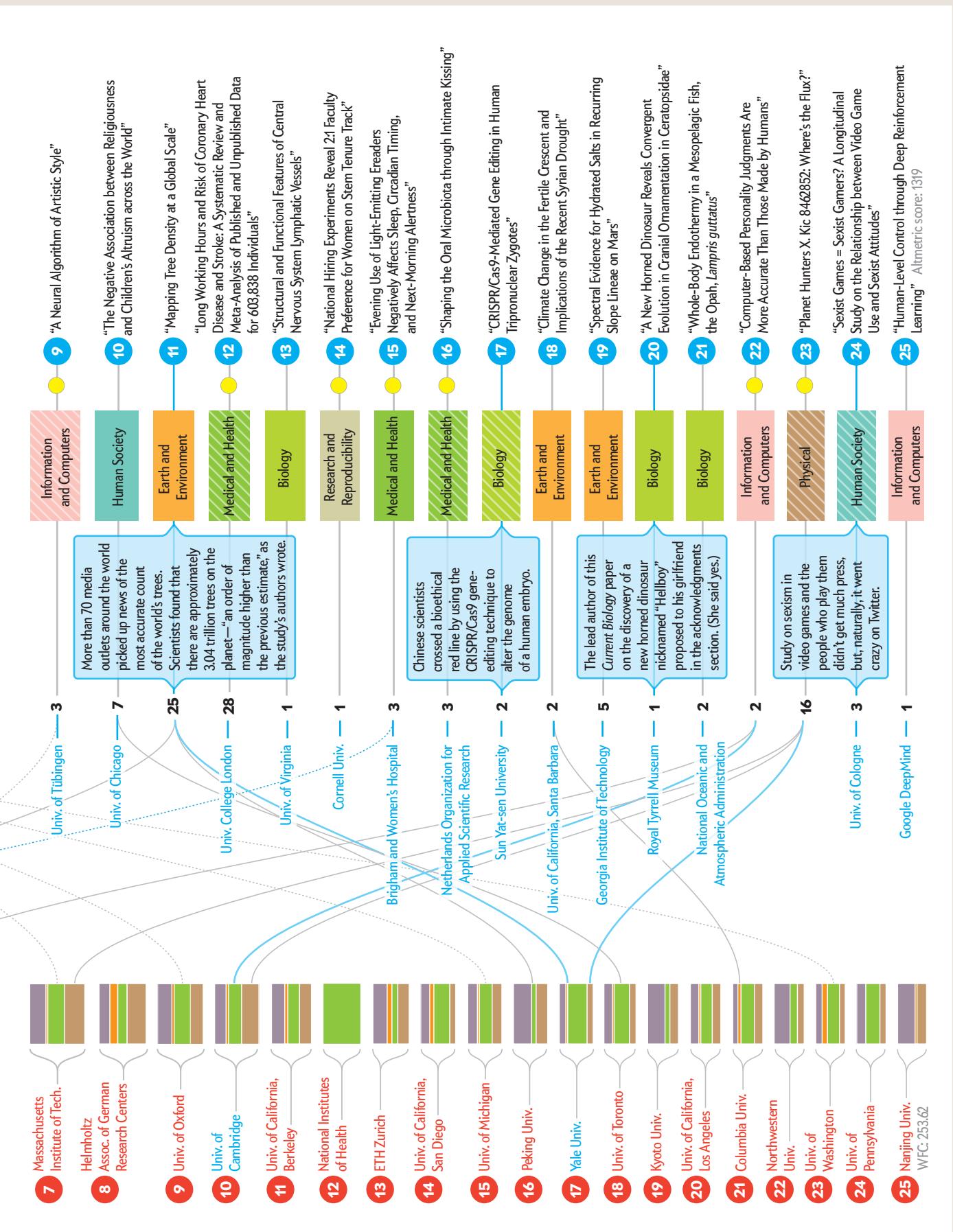
The 25 most talked-about studies of 2015, as ranked by Altmetric.

INSTITUTION

LEAD AUTHOR'S INSTITUTION

ARTICLE TITLE





*The Nature Index ranked the output of institutions by analyzing research articles published in 2015 in 68 high-quality science journals. Weighted fractional article counts provide a way of measuring the contribution of each institution to the total body of research while avoiding overrepresentation by astronomy and astrophysics journals. It is compiled by Nature Research, which, like Scientific American, is part of Springer Nature.

#Altmetric scores scholarly journal articles according to the reach, as measured by data including mentions in the news and on social media. It and Scientific American are partly owned by Holtzbrinck Publishing Group.

†Some articles in Altmetric's top 25 were not in the Nature Index, either because they were published before 2015 or because they did not appear in the 68 journals tracked by the Nature Index.



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Devin Powell is a freelance science journalist living in New York City. His work has been published by the *New York Times*, the *Washington Post*, *Nature*, *National Geographic*, *Smithsonian* and a variety of other news outlets.

SCIENCE AND SOCIETY

THE PLIGHT OF THE CELEBRITY SCIENTIST

Engaging the public has long been taboo in scientific circles, but social media outlets are starting to force a change

By Susana Martinez-Conde,
Devin Powell and
Stephen L. Macknik

ROGER SMITH (NOT HIS REAL NAME) never meant to become a popular scientist. But he saw no reason to avoid reporters a few years ago after publishing a major discovery in the research journal *Science*. Suddenly, his work was featured everywhere, including in the *New York Times*. Prestigious “ideas” conferences invited him to speak, and he found that he had a knack for explaining science to a general audience. His online TED talk attracted hundreds of thousands of views.



Increasing fame brought unexpected problems, however. Although Smith continued to conduct high-quality research, and prestigious scientific journals regularly published his results, several of his peers in the scientific community began punishing him for his growing celebrity. Smith's applications to fund new experiments started getting rejected. The anonymous reviewers who evaluated his grant proposals made "terrible comments," he recalls, such as "the 'very well publicized' or the 'overexposed' work of [Smith]." In response to the backlash, he declined an invitation to give a second TED talk and closed his laboratory to the press.

"That's it," he remembers thinking at the time. "I'm not communicating [with the public] anymore."

The kind of professional retaliation that Smith experienced is commonly known as the Sagan effect, named for astronomer and superstar science popularizer Carl Sagan. Largely as a result of his growing public profile, Sagan suffered ridicule among his peers and lost out on various professional opportunities, including tenure at Harvard University in the 1960s and membership in the National Academy of Sciences in the 1990s. "People said that he was spending more time popularizing than doing serious research," says Joel S.

Levine, now a professor at the College of William & Mary, who disagreed with the gossip. The two became friends when both worked on the Viking program in the 1970s.

A quarter of a century after Sagan's letdown at the National Academy of Sciences, his eponymous effect continues to persist. A number of studies over the past few years indicate that scientists as a group still discourage individual investigators from engaging with the populace unless they are already well-established, senior researchers. Such a mind-set deprives society of the full range of expertise it needs to make informed decisions about some of the most complex issues of the day—from genetic engineering to climate change to alternative forms of energy. The silencing of voices in the scientific community also leaves important questions about policy and the economy vulnerable to fact-challenged spin doctors of every political persuasion. Fewer scientific voices, for example, mean fewer arguments to counter antiscience or pseudoscientific discourse.

By limiting public engagement to the most seasoned researchers, the Sagan effect also perpetuates the impression that science is the domain of older white men, who dominate the senior ranks. Although the proportion of full professors who are women has increased steadily over the past couple of decades, and the number of minorities in top positions has grown (albeit not as quickly), diminishing the public presence of these groups might discourage women and underrepresented minorities from even considering careers in science.

We recently contacted nearly 200 active scientists who regularly engage the public—as sought-after speakers, influential blog writers or best-selling authors. We wanted to learn how many of these elite popularizers faced professional blowback over their outreach efforts and under what circumstances. In addition to being consistent with

previous peer-reviewed research, our informal survey revealed that a welcome change in culture might finally be at hand. The increased use of social media outlets such as Twitter, Facebook and personal blogs, among other changes in the scientific world in recent years, seems to be breaking down some of the long-standing barriers to greater dialogue between researchers and the community at large.

BACHELOR SCIENTISTS

TO A CERTAIN EXTENT, the Sagan effect traces its roots to a centuries-old view of how scientists are supposed to work. At the height of the scientific revolution in the 1600s, for example, many researchers followed the example of Sir Isaac Newton, who was intensely dedicated to the development and investigation of physics and mathematics and never married. These bachelor scientists (and they were nearly all men) were seen as pure seekers of truth who were not distracted by the more mundane concerns of having a family.

Something of that ethos continues to the present. Whereas today's scientists are much more likely to be married and even to have children, they are still supposed to be devoted to life in the lab, at least according to many graduate school advisers and mentors. Thus, anything that takes them away from their research—such as having a hobby or participating in public debates—can undermine their credibility as researchers. Although few studies have addressed the professional consequences of science popularization across the globe, the research that does exist suggests that the Sagan effect is still a problem.

Unrealistic expectations, however, explain only part of the behavior. Many of the researchers we interviewed for this article suspect that professional jealousy also fueled some of the backlash they experienced. "A lot of this happens

behind your back," Frans de Waal, a renowned primatologist at Emory University, wrote in an e-mail. He added that he generally hears indirectly, from friends, about colleagues complaining about his popular work.

Two of us (Martinez-Conde and Macknik) have experienced similar criticisms of our outreach efforts. At an annual performance review when Martinez-Conde worked in a previous institution, the chair of her department complained that her "stellar" academic productivity that year had been overshadowed by her mainstream science writings. Official feedback on one of Macknik's grant applications to the National Institutes of Health advised that his science communication was excessive.

Although our careers did not suffer overall, we became curious about other scientists' experience. We teamed up with co-author Devin Powell and contacted 190 elite communicators by e-mail and telephone and in person. We received 81 responses. Whereas many scientists reported that their outreach efforts had been a positive force in their careers, others had experienced a mixed bag of positive and negative consequences. And some, such as Smith, saw largely negative effects.

A few investigators had found creative solutions to the dilemma by, in effect, leading double lives. Roboticist Dennis Hong of the University of California, Los Angeles, for example, says he is a superstar in South Korea, where he grew up, but keeps quiet about his celebrity in the U.S. "In Korea, people recognize me. They want to take pictures," he says. "These days I have two modes: outreach in Korea but no outside activities in the States. In the research community, in academia, if you're too much exposed, if you're always on TV, always on the cover of magazines, the perception is that you're not a true researcher."

SURPRISING EVIDENCE

THE COMMON ASSUMPTION of the research community that popularizers cannot be serious scientists falls apart when one looks at the evidence. Multiple studies to date suggest that far from being second-rate investigators, researchers who regularly engage the public are more productive in the lab as well.

A 2008 study of more than 3,600 researchers at the French National Center for Scientific Research, for example, found that active disseminators of science had more peer-reviewed publications and their work was cited more often by other investigators than nondisseminators.

Another study measured the numbers of scientific papers and popular science articles published from 2005 to 2007 by scientists in Argentina, Australia, Brazil, Canada, Finland, Germany, Hong Kong, Italy, Malaysia, Mexico, Norway, the U.K. and the U.S. The results indicated that scientists with popular science writing credits were more prolific academic writers and worked harder than most of their peers (an average of 49.3 versus 47.8 hours per week). Sagan himself matched this profile: he averaged more than one scientific publication a month over the course of his 40-year career, until his death in 1996.

We had expected that the successful science popularizers who answered our survey would be supportive of junior researchers following their lead. But even they sometimes cautioned that most researchers who want to achieve tenure should probably delay interacting with the general public until after they have secured their university position. Daniel Kahneman, who won a Nobel prize for economics in 2002 and published the best-selling book *Thinking, Fast and Slow* in 2011, says that becoming a public figure too early in one's career challenges the norms of the scientific community. Fame should come from scientific publi-

cations, he argues, not engagement with the public. "If you're writing books for a general audience while you're an assistant professor, it's likely you won't get tenure because you're not serious," Kahneman says. "When you're talking about research universities, that's the rule. You're supposed to do research until you get tenure and quite a bit later."

Daniel Gilbert, a professor of psychology at Harvard and author of *Stumbling on Happiness*, agrees. "I started [writing for popular consumption] in 2000, when I was a full, tenured professor at Harvard," he says. "I wouldn't advise young, untenured professors to do this."

Yet unintentionally, the net result of this "wait until tenure" caution often ends up hurting women and minorities because they are not well represented at the top ranks of academia. Perhaps partly as a result of this lack of representation, some minority academics find themselves under intense institutional pressure to communicate—whether they have an inclination for it or not. "In essence, this amounts to an additional job that they are expected to do because of their background (rather than their desire to participate in public communication)," Lucianne Walkowicz, an astronomer at the Adler Planetarium, wrote in an e-mail.

"If you're articulate, if you look halfway decent on camera, you get asked to do this," says J. Marshall Shepherd, who is African-American, directs the atmospheric sciences program at the University of Georgia and hosts his own television show. Raychelle Burks, an assistant professor of chemistry at St. Edward's University in Austin, Tex., jokes that she sometimes feels as though journalists find her by Googling "minority scientist." "As a black woman, I'm all for getting opportunities," she says. "But there's a difference between 'Are you the best person for the job?' or

'Are you a token?' because someone said, 'We need a person of color.'"

CHANGING NORMS

SOME OF THE RESPONSES to our survey suggest that engaging with the rest of society is becoming less hazardous to a scientist's career—and can prove beneficial. So many people have social media accounts these days that becoming a public figure is just not as unusual for scientists as it once was. Further, as traditional sources of funding continue to stagnate, "going public" sometimes leads to new, unconventional revenue streams for worthy projects.

The social media explosion of the past decade has nonetheless exposed a generational rift between digital natives and older investigators. "I've heard 'What are you doing on Twitter? That's a waste of time,'" says Chris Gunter, a professor at Emory School of Medicine who goes by the handle @girlscientist. "But I had a paper come out in *Nature* in 2014 that started as a discussion on Twitter."

Nevertheless, our survey suggests that a handful of forward-looking institutions (such as Emory and the Massachusetts Institute

of Technology) may have begun to appreciate outreach as a core area of academic performance—in addition to the traditional roles of research, teaching and administration. "At Emory during my mid-term review, I had really made it clear to my own institute what I was doing," says Jaap de Roode, a biologist who studies parasites. "They said it was a very positive thing for me and for the university. It gives a lot of visibility."

Exceptional among federal funding agencies, the National Science Foundation has adopted an official position in favor of popularization. In addition to intellectual merit, grant proposals to the foundation are also evaluated for their "broader impacts" on society, including the wide dissemination of research findings to the public. Less friendly organizations and senior researchers should follow these examples.

Only by communicating our discoveries widely can we, as scientists, climb down from our ivory tower and play a larger role in shaping the kind of society in which we wish to live—one that values facts, encourages scientific endeavors and continues to grow. ■

MORE TO EXPLORE

HOW TO SPIN THE SCIENCE NEWS

The Embargo Should Go. Vincent Kiernan in *Inside Higher Ed*. Published online August 21, 2006. www.insidehighered.com/views/2006/08/21/embargo-should-go

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Embargo Watch: <https://embargowatch.wordpress.com>

The FDA's news media policies: www.fda.gov/NewsEvents/Newsroom/NewsEmbargoPolicy/default.htm

THE PLIGHT OF THE CELEBRITY SCIENTIST

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Scientists Who Engage with Society Perform Better Academically. Pablo Jensen et al. in *Science and Public Policy*, Vol. 35, No. 7, pages 527–541; August 2008.

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Gap between Science and Media Revisited: Scientists as Public Communicators. Hans Peter Peters in *Proceedings of the National Academy of Sciences USA*, Vol. 110, Supplement No. 3, pages 14,102–14,109; August 20, 2013.

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FROM OUR ARCHIVES

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WEATHER

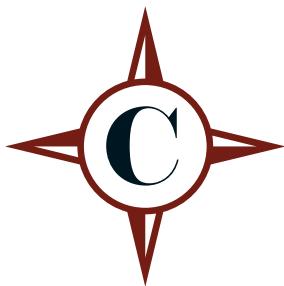
On the Trail of El Niño

This fickle and influential climate pattern often gets blamed for extreme weather. A closer look at the most recent cycle shows that the truth is more subtle

By Emily Becker







ALIFORNIA GROWS MORE THAN 90 percent of the tomatoes, broccoli and almonds consumed in the U.S., as well as many other foods. These crops require a lot of water. In the spring of 2015, after four years of little winter rain, the state was in a severe drought. Reservoirs were far below capacity, and underground aquifers were being heavily tapped. Mountain snowpack, an important source of meltwater throughout the spring and summer, was nearly gone in many areas.

Not surprisingly, then, when the National Oceanic and Atmospheric Administration announced that an El Niño climate pattern was setting up over the Pacific Ocean, California farmers and their neighbors took note. Conventional wisdom said that El Niño brings plentiful rains to the Golden State.

El Niño is the warm half of a cycle of warming and cooling in the tropical Pacific Ocean's surface waters. The cycle recurs about every three to seven years; the cool half is called La Niña. When either phenomenon arises, it generally prevails for six months to a year. During El Niño, the warm waters heat the air above them, causing changes to the atmospheric circulation that affect the entire world. NOAA, where I conduct climate research, can usually see an El Niño or La Niña coming in advance of when it will have its strongest influence on global weather.

Californians' hopes were high, and yet the effects that usually occur with an El Niño there and elsewhere do not happen all the time. During the 20 El Niño seasons since NOAA began tracking them in 1950, only about half brought above-average precipitation to California during its rainy season: December, January and February. In some cases, the effects are the opposite of what is expected. Forecasters have become good at predicting a developing El Niño or La Niña, but they still struggle with predicting the regional weather changes that might result.

In early 2015, as California dried out further, forecasters faced several burning questions: Would the coming El Niño be a big one? Would it save California? For that matter, would it amp up hurricanes in the Pacific and reduce hurricanes in the Atlantic, bake Australia, fuel forest fires in Indonesia, or make the upcoming winter disappear in the Northeast, as some El Niños had done in the past? And could we know ahead of time?

Emily Becker is a contract research scientist at the National Oceanic and Atmospheric Administration's Climate Prediction Center in College Park, Md., where she specializes in climate diagnostics and prediction. She also writes a monthly blog at NOAA that tracks El Niño, La Niña and other climate phenomena.



Being able to answer such questions would greatly help farmers, forecasters, emergency planners and the general public prepare for extreme weather, and investigators are trying hard to pin down the data that are needed. Yet as the tale of how the most recent, extreme El Niño unfolded demonstrates, the science is tricky.

MARCH 2015: EL NIÑO IS HERE

EARLY SIGNS of a developing El Niño occur under the ocean surface. Winds across the tropical Pacific typically blow from east to west—the trade winds that reliably have carried sailing ships across the great ocean. These winds keep the surface water in the eastern and central Pacific slightly cooler and pile up warm water in the western side, toward Indonesia. Occasionally these winds can weaken, allowing slow waves of warmer western waters to begin to travel back eastward along the equator toward South America over many months. That can kick off an El Niño or feed one that has already begun.

To me and other meteorologists, it looked like the developing 2015 El Niño was going to be a big one. Over the past several months we had seen sea-surface temperatures that were warmer than average in the tropical Pacific, including the Niño 3.4 region in the central Pacific, which we track as a leading indicator. El Niño, though, is part of a phenomenon that couples changes in the ocean to changes in the atmosphere—the El Niño/Southern Oscillation—so we were also monitoring the atmosphere for signs that it was responding to those increased ocean temperatures.

Water even just a few degrees higher than usual holds a tremendous amount of heat, which warms the air above the ocean, coupling the changes in the ocean to the atmosphere. During El Niño, the warmer central-eastern Pacific takes over as the engine affecting an atmospheric pattern called the Walker Circulation [*see box on opposite page*]. With a strong source of rising moist air now much farther east, the surface winds weaken, sometimes reversing altogether and blowing west to east. This atmospheric reaction is the Southern Oscillation, and it is essential to El Niño, helping it sustain and strengthen itself.

In March the effects of the warmer tropical Pacific had taken

IN BRIEF

The media, and even meteorologists, tend to say that certain kinds of extreme weather are caused by El Niño or La Niña, but the patterns are not always consistent. For example, the 2015–2016

El Niño did not bring expected heavy rains to southern California, much needed to reduce the drought there.

The 2015–2016 El Niño was among the three strongest ever recorded. It af-

fected weather across the globe, including a warmer winter in the northeastern U.S. But global warming, as well as other climate patterns, could have also contributed.

Forecasters predict La Niña will prevail during the 2016–2017 winter, which often happens after a strong El Niño. La Niña also increases the probability of some extreme events.

Cause and Effect

An El Niño or La Niña climate pattern arises when Pacific Ocean temperatures change, relative to neutral conditions (illustrations). In winter 2016 a strong El Niño altered the jet stream across the U.S. and made precipitation more or less likely in certain regions worldwide (map).

El Niño or La Niña?

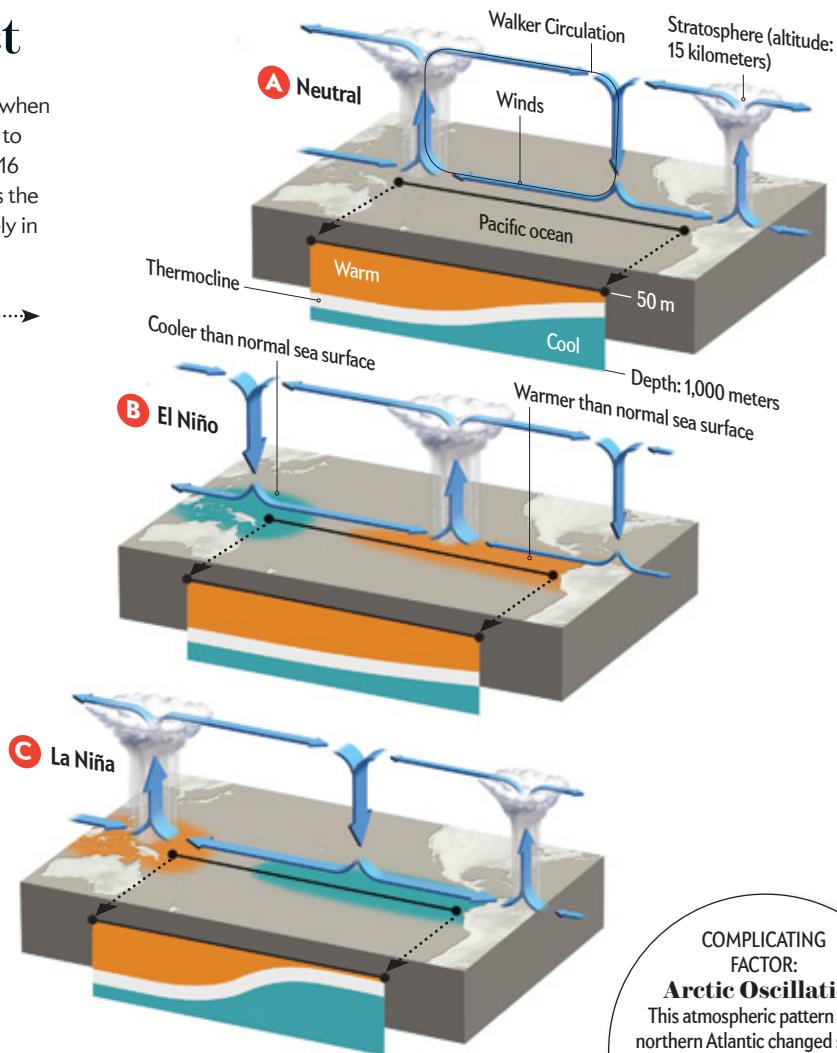
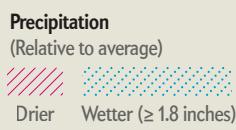
Warm water in the western Pacific A typically heats air that rises, rains out and circulates eastward when it hits the stratosphere. It descends and travels west, helping to trap warm water there. If the surface winds weaken over several months, warm water can drift back eastward, changing the Walker pattern and pushing warm water down deeper, kicking off an El Niño B. If the east-west surface winds get stronger instead, even more warm water moves west and deepens there as well, setting up La Niña C. The atmospheric reaction to these water flows, ever changing over a time frame of months, is called the Southern Oscillation.

What Happened in 2016

El Niño helped to push the subtropical jet stream's path across the U.S. south in early 2016. The shifting jet, and a changing mix of warm and cool seawater (yellow and blue), led to enhanced or limited precipitation in certain regions (blue and pink pattern overlays). Other factors also influenced global weather, however, as they do every year.

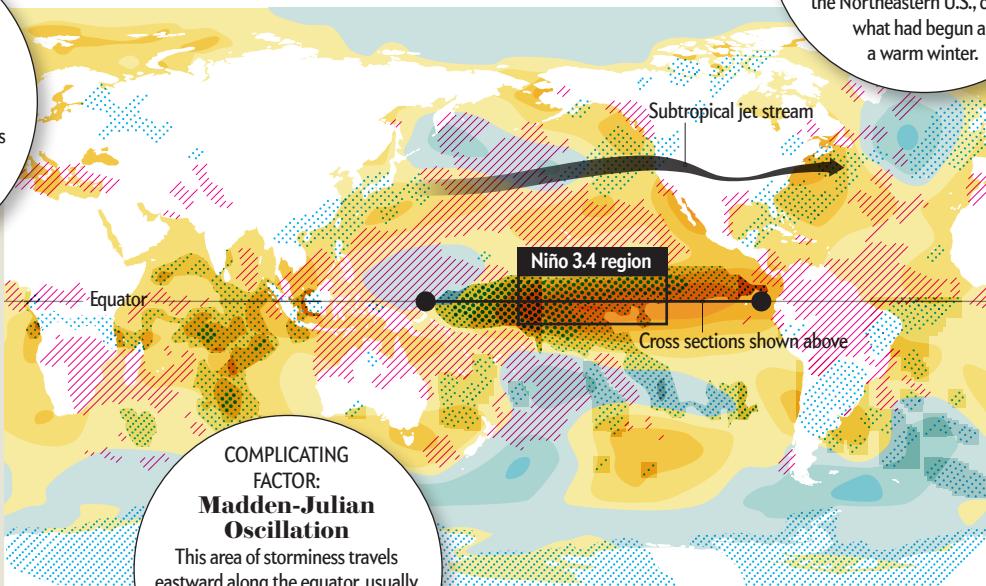
COMPICATING FACTOR: Climate Change

As the atmosphere and oceans warm overall, that could change the nature of El Niño and La Niña, as well as how much those patterns may affect local weather, but meteorologists are not yet sure how.



COMPICATING FACTOR: Arctic Oscillation

This atmospheric pattern in the northern Atlantic changed state as 2016 began, allowing cold air up in the Arctic to drift down into the Northeastern U.S., cooling what had begun as a warm winter.



COMPICATING FACTOR: Madden-Julian Oscillation

This area of storminess travels eastward along the equator, usually crossing the Pacific in a few weeks. It temporarily strengthened and weakened El Niño's impacts in winter 2016.



hold. The Walker Circulation was weakening. We also saw bursts of westerly wind over the tropical Pacific, which can encourage warmer surface waters to move eastward. Heat deeper in the Pacific Ocean was high, too, which could help extend the atmospheric coupling. After 12 months of watching, NOAA issued an El Niño Advisory. Game on.

MAY 2015: PROBABILITIES RISE

BY MAY, NOAA had determined there was a 90 percent chance that the current El Niño would continue through the summer and an 80 percent chance that it would continue through the end of 2015. The agency was confident in its prediction because sea-surface temperatures in the equatorial Pacific remained substantially above average during April. The same was true for water below the surface, in the upper 300 meters of the ocean. The atmospheric response had strengthened, too.

But what weather effects might we see? And what would happen in California? El Niño typically exerts its strongest impacts on temperature and rain in the early winter, which was still six months away. Some signs suggested that this El Niño would be like other strong ones in the past. Drought and heat waves in Australia were rearing up (autumn was giving way to winter there). And the western Pacific cyclone season was off to a roaring start, with seven named storms by May; the average is two.

JULY 2015: FULL SWING

AS JULY COMMENCED, nearly all the computer models were in agreement, and the ocean and atmosphere continued to behave according to plan. El Niño was well established, and forecasters were convinced that it would become very strong. The three-month-average sea-surface temperature in the Niño 3.4 region was expected to peak near an all-time high, matching that of the two previous, strongest El Niños on record: 1997–1998 and 1982–1983.

Southern Californians who remembered the 1997–1998 winter anticipated pounding storms and surf. During the 1982–1983 and 1997–1998 El Niños, winter conditions shifted the Pacific subtropical jet stream—a band of eastward-flowing air

EL NIÑO'S EFFECTS can be inconsistent. In winter 2016 it did not bring extra rain to central California as hoped, offering no help to a years-long drought (1). But heavy snow in the mid-Atlantic states, like the January 2016 blizzard, has happened during El Niños before (2).

high in the atmosphere above the U.S. that often influences weather—south toward southern California. Powerful storms, fed with moisture from the warmer waters, provided heavy, reservoir-filling rains—as well as landslides along a soggy coast.

Farmers and residents hoped that the new El Niño would deliver plentiful precipitation by December. Forecasters gave a 60 percent chance that during the upcoming 2015–2016 winter, regions of southern California, as well as the Gulf States, would see rain amounts in the upper third of the historical record. This forecast was derived in part by monitoring several different signals, including El Niño, and comparing them with past trends to see if the odds of a certain outcome might be shifting.

OCTOBER 2015: UNEXPECTED WINDS

IN OCTOBER, hope for California was high. We were closing in on the peak of the 2015–2016 El Niño, and it still ranked among the strongest in our records. Yet we were seeing something unexpected. The surface winds along the Pacific equator, important for maintaining the high sea-surface temperatures, had not weakened as much as they had during past strong El Niños. In 1997–1998 the winds weakened so much they reversed, blowing from west to east during October and November, moving even more warm water from the far western Pacific into the central Pacific and feeding the El Niño.

We humans have a tendency to expect that the outcome of a set of circumstances will always be the same, but variability happens in nature all the time. In coastal northern California, a strong El Niño year averages about 40 rainy days per winter, compared with about 26 during a non-El Niño winter. Yet the winter of 1965, one of the six strongest El Niños, had fewer rainy days than the non-El Niño average. In these times of global warming, we also had to wonder whether that was playing a

role, too. If it was, prediction of El Niño's effects would become that much more difficult.

JANUARY 2016: A LOT GOING ON

BY JANUARY, El Niño had put up some impressive numbers. In December the Niño 3.4 index broke the record for that month at 2.32 degrees Celsius above average, surpassing the 2.24 degrees C of December 1997. El Niño is ultimately measured on seasonal timescales, though, so the average of the sea-surface temperature anomaly (the departure from the long-term average) over three months is what we really pay attention to. From October to December 2015, the anomaly was 2.3 degrees C, tied for first place with 1997.

Outside of California, the effects of El Niño were mostly occurring as expected. Much more rain than is typical fell in eastern Africa during the "short rains" season (October through December). Southern Africa had continued dry conditions. Uruguay, southern Brazil and Paraguay experienced a lot of rain, and northern South America had been dry.

Australia's typical El Niño impact is dryness over most of the continent from about July to December, but in 2015 there had not been a clear rainfall deficit, except in parts of eastern Australia. It is possible that a record warm Indian Ocean had a strong counter-effect—a reminder that the climate system has many moving parts, so expected impacts from El Niño are not guaranteed.

Closer to home, the Northeast was very warm, as anticipated. Michelle L'Heureux, my fellow meteorologist at NOAA, wrote in her blog: "For the first time ever my extended family did our Christmas gift exchange outside on my aunt's patio in the Washington, D.C. area.... We abandoned hot cider in favor of tropical beverages. Some of us wore t-shirts and sandals. We played catch with the dogs."

As in Australia, El Niño was not the only cause of the unusual weather in Washington. An atmospheric pattern known as the Arctic Oscillation—epitomized by the "polar vortex" of winds that circle the Arctic—had entered a strong state. Unlike some recent winters, when the vortex was weak and allowed cold air to pour down into the U.S., during December 2015 it had been strong, trapping the frigid air way up north and allowing warm air from the southern U.S. to drift northward.

Several other non-El Niño oceanic and atmospheric phenomena could also have influenced weather in one part of the globe or another. One is the Madden-Julian Oscillation (MJO), an area of storminess that circles the equator, traveling eastward and lasting for weeks. It can temporarily enhance the effects of El Niño but can also reduce them. As I wrote in January, "Clearly, the question of how the MJO and El Niño act to reinforce or weaken each other is still up for debate."

Then there is the Pacific Decadal Oscillation, a relation between the surface temperatures of the eastern and western North Pacific that often prevails for 15 years or more before switching to a different state. All these patterns affect one another. And of course, climate change is a wild card that could influence any of these patterns in still unpredictable ways.

L'Heureux's warm Christmas, and the extremely warm November and December across eastern North America, seemed to stem from a combination of El Niño, the bottled-up cold air near the Arctic and an active Madden-Julian Oscillation, plus a large component that cannot be explained even by those fac-

tors. Despite screaming headlines in daily newspapers and bold declarations by television weather forecasters, all saying El Niño was causing the extreme weather, it is not possible to point to a single storm, or cold snap, or heat wave and say, "That's El Niño." El Niño influences the background state, so a collection of weather events can be partially attributed to El Niño but not a single incident.

In California hopes were quickly disappearing that El Niño would help ease the drought. The rain in December and early January had been above average in northern California but around average in the southern half of the state. A brief string of storms coming from the Pacific finally arrived in the last three days of January, delivered by a so-called atmospheric river of moisture that heads directly toward the U.S. West Coast from the tropics. It dropped a fair amount of snow across the Sierra Nevada Mountains, which might, it was thought, be beneficial when it melted later in the spring.

"Of course, one wet month isn't going to erase California's drought," wrote another of my NOAA colleagues, Tom Di Liberto, in his own climate blog. "While some interior portions of California as well as northern California have recorded above-average precipitation, areas to the south, including the heavily populated coastal corridor stretching from Santa Barbara to San Diego, have seen precipitation less than 75% of normal." Rainstorms, he concluded, will "need to occur more often to get this year back to normal," let alone overcome reservoir and aquifer shortfalls that have accumulated since 2011.

Even a strong El Niño is no guarantee of abundant rainfall for California. It just tilts the odds in favor of a wetter-than-average winter there.

After the warm Christmas in the mid-Atlantic, snow hit there in January, shutting down Capitol Hill for two days. Weird weather once more. The public was ripe for hype about El Niño, but again, attributing a single storm to one climate influence, especially such a complicated nor'easter, just cannot be done. Although at least six of the top-10 snowstorms on record in Washington, D.C., have occurred during El Niño conditions, a lot of components had to come together to create the 2016 blizzard. They included a cold snap, warm Atlantic waters to feed moisture to the storm and a strong frontal system. El Niño's fingerprint may have been present in some of those factors, but it is tough to separate out. During El Niño, the subtropical jet stream does tend to steer storms across the Gulf States, as well as Georgia and the Carolinas, but they typically exit to the Atlantic south of Maryland and Virginia. Yet during some storms the jet stream bends more northward to D.C., which is somewhat unusual for El Niño conditions but not unheard of.

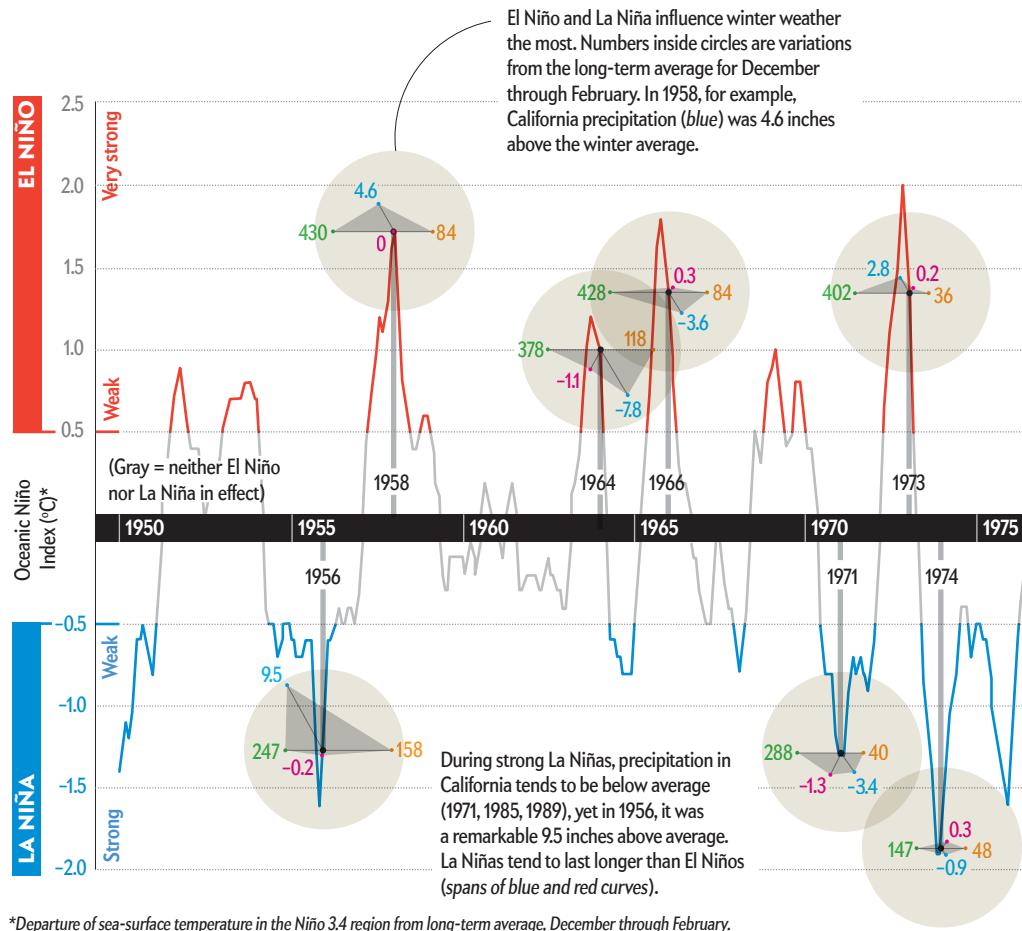
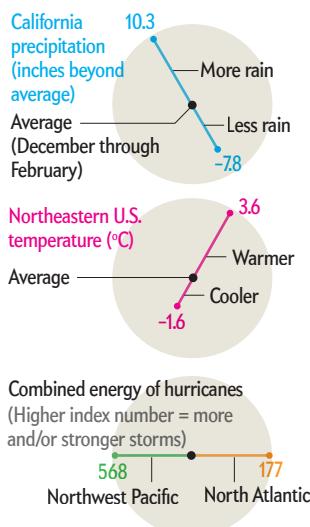
MARCH 2016: THE BIG THREE

WE HAD SEEN ENOUGH by March to address the widespread claims in popular media that the U.S. and the world were experiencing the strongest El Niño ever. We had a complete data set for 2015–2016 and could compare it with data for the other two biggest El Niños: 1982–1983 and 1997–1998. It was definitely *one* of the strongest three going back to 1950, but ranking El Niños is difficult because strength can be measured in different ways.

The primary number we use at NOAA is the Oceanic Niño Index, which shows how the three-month-average sea-surface temperature in the Niño 3.4 region departs from the long-term

Did El Niño Do That?

El Niños (red) and La Niñas (blue) sometimes do not generate the extreme weather we expect, such as a wet California winter (values inside circles), even though some meteorologists and headline writers are tempted to blame these patterns.



average temperature. That value for November 2015 to January 2016 was 2.3 degrees C, tied with 1997–1998. We watch other areas of the oceans, too, including the eastern Pacific (warmer in 1997–1998) and the western Pacific (warmer in 2015–2016). And we consider the second part of the El Niño/Southern Oscillation, which is the all-important atmospheric response to ocean temperatures. Overall, the atmospheric response during 1997–1998 was stronger than during 2015–2016.

As for the winter weather and climate, a number of similar outcomes had arisen in all three cases, but there were also some notable exceptions [see box above]. Among them: Northern California took most of that state's rain instead of southern California. Determining why this pattern was different from past strong El Niño winters will keep climate researchers busy for years to come. Many potential components are at play, including that the world's oceans today are much warmer than they were during the past two strong El Niños. And short-term chaotic effects are always present in weather systems, which ensures that even if one El Niño looks identical to another, its effect on the weather will not necessarily be the same.

ENTER LA NIÑA?

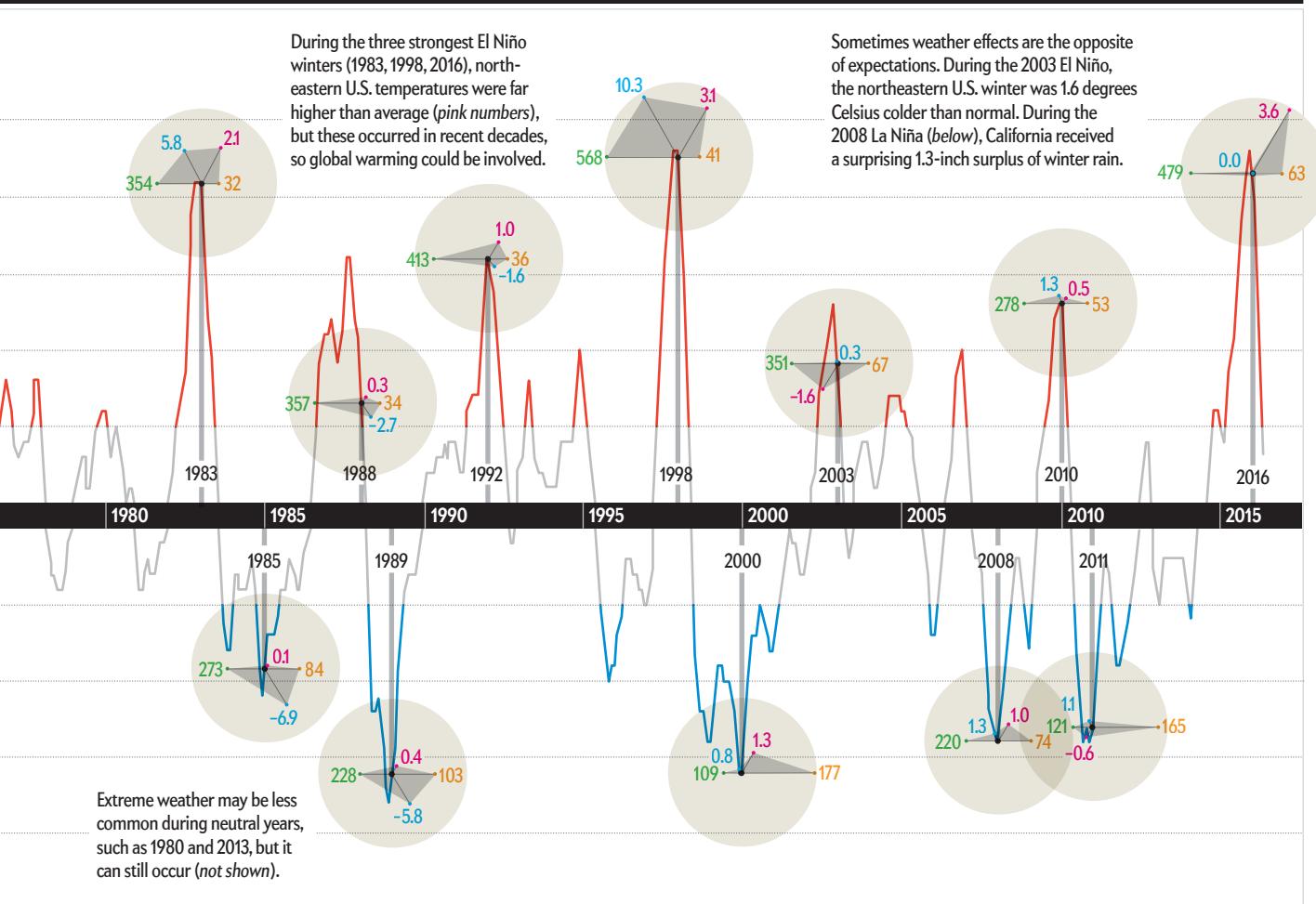
A YEAR AFTER NOAA first announced El Niño conditions, the episode was ending. Sea-surface temperature anomalies across

most of the equatorial Pacific had decreased in February 2016, and the large amount of water below the surface that was warmer than average declined, too.

In March it was also looking likely that conditions would transition to neutral by early summer, with about a 50 percent chance that La Niña would set in by the fall. La Niña conditions have followed six of the 10 moderate and strong El Niños since 1950, but that sample size is too small for a confident forecast.

Our computer climate models also have a difficult time making accurate forecasts in spring (specifically, March through May), when El Niño and La Niña are often weakening, changing into neutral. Weather over North America during this transition season is highly variable, which often overwhelms signals from either phenomenon.

Nevertheless, most models agreed that La Niña would develop by the fall of this year. In April, NOAA issued a La Niña Watch, and by August we had determined that there was a 50 percent chance that La Niña would be in place by the fall. Computers, crunching the latest data, found that sea-surface temperatures in the Pacific would continue to drop, potentially passing the La Niña threshold (0.5 degree C below average). Also, cooler than average water was accumulating under the surface across the entire Pacific, along the equator. It is interesting to note that subsurface water in the Niño 3.4 zone reached



record-cold temperatures in 1998—immediately following the strong El Niño of 1997–1998.

In the U.S., La Niña impacts are roughly the opposite of El Niño's but not precisely. La Niña alters westerly winds and the jet stream in its own ways. Among other things, it tends to create a hospitable environment for hurricanes to develop in the Atlantic. NOAA's official Hurricane Season Outlook update, which was released in August, forecast a typical to above-average North Atlantic hurricane season because other factors were at play. La Niña winters in California tend to be dry.

OSCILLATION

DESPITE EL NIÑO's fearsome reputation, it does not usually trigger a greater number of weather-related disasters worldwide than other years do, but the disasters are more predictable. If government and emergency planners take heed of El Niño-related seasonal forecasts, it may be possible to move resources to certain places, ahead of disasters, to reduce the human impacts should a given El Niño produce its typical effects.

Researchers are still not clear on how global warming will interact with the El Niño/La Niña cycle. Some work suggests that warmer overall oceans will lead to more powerful El Niños, but other studies say that global warming could actually reduce their strength. Because the entire global system includes large atmo-

spheric and oceanic phenomena that naturally flip between different states, such as the Pacific Decadal Oscillation, figuring out how El Niño has been affected by global warming so far, and how it could be in the future, has been a challenge. Researchers will continue to try to decipher possible connections.

One thing we can say for near certain is that El Niños and La Niñas will continue to occur, some stronger than others. Evidence from fossilized corals tells us that the cycle has been recurring for thousands of years. As we better understand climate system dynamics, we can better anticipate the effects of this important pattern on global weather and on people around the world. ■

MORE TO EXPLORE

International Research Institute for Climate and Society's ENSO Web page: <http://iri.columbia.edu/our-expertise/climate/enso>

NOAA's El Niño/Southern Oscillation (ENSO) information Web page: www.climate.gov/enso

NOAA's ENSO Blog: www.climate.gov/news-features/department/enso-blog

Pacific Marine Environmental Laboratory's ENSO Web page: www.pmel.noaa.gov/elniño/what-is-el-nino

FROM OUR ARCHIVES

The Jet Stream Is Getting Weird. Jeff Masters; December 2014.

DEATH GRIP: New Zealand's lizardlike tuataras face threat of extinction from climate change.



HOME OFF THE RANGE

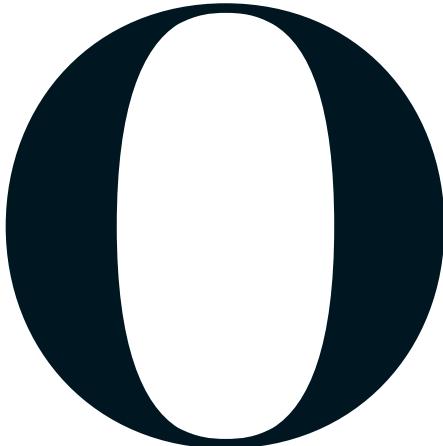
To save species under threat from climate change, scientists are looking to move them to areas they have never inhabited before—a strategy fraught with risk

By Richard Conniff





Richard Conniff is an award-winning science writer for magazines and a contributing opinion writer for the New York Times. His books include *House of Lost Worlds* (Yale University Press, 2016) and *The Species Seekers* (W.W. Norton, 2010).



N A KNOB OF ROCK IN THE COOK STRAIT KNOWN AS NORTH BROTHER Island, a population of the lizardlike creature called the tuatara is quickly becoming all male. When scientists examined the imbalance in the late 1990s, the sex ratio was already 62.4 percent male, and it has rapidly worsened since then, to more than 70 percent. Researchers say climate change is the cause: ground temperature determines the sex of tuatara embryos,

with cooler temperatures favoring females and warmer ones favoring males. When climate pushes the sex ratio to 85 percent male, the North Brother tuataras will slip inescapably into what biologists call the extinction vortex.

For the tuatara and many other species threatened by climate change, relocating them to places they have never lived before—a practice known as assisted colonization—is beginning to seem like the only option conservationists have for saving them. “We’d prefer to do something a little more natural,” says Jessica Hellman, an ecologist now at the University of Minnesota, who was among the first researchers to put the idea of assisted colonization up for discussion. That is, it would be better for species to shift their ranges on their own, using natural corridors to find new homes as their old ones become less habitable. But for many island and mountain species, long-distance moves were never an option in the first place, Hellman explains. In other cases, old corridors no longer exist, because human development has fragmented them.

The idea of assisted colonization as a conservation tactic has elicited fierce criticism, however, because of its potential to wreak ecological havoc on both the relocated species and the destination habitat. In addition, many conservationists have devoted their lives to putting species back where they used to live 100 or 200 years ago—gray wolves in Yellowstone or bison on the Great Plains. Imagining new places where they might live in some unknowable future can feel like heresy.

But as the likely devastation from climate change has become

more apparent, criticism has given way to guidelines on how and when to move species—and to increasing, if uneasy, acceptance of assisted colonization. A recent survey of 2,300 biodiversity scientists in the online journal *Elements: Science of the Anthropocene* found that most supported the idea under certain limited conditions, notably when it would prevent extinction and when the risk to the destination habitat is small or nonexistent.

OUT OF BOUNDS

THE NEED TO PLAN WHAT COULD BE, in essence, emergency evacuations of species became painfully evident last November, when a wildfire devastated the habitat of one of the world’s most endangered mammals—a small, kangaroo-like marsupial called the Gilbert’s potoroo—in a drought-stricken area of Western Australia. The fire killed 15 of the estimated 20 potoroos in the reserve where the species had been rediscovered in 1994 after having previously been considered extinct for more than a century. Loss of that habitat would have been an automatic sentence to extinction, except that, in the aftermath of the rediscovery, conservationists had established a separate colony of the species nearby.

The potoroo was translocated within its original home range, which is much less controversial than moving it into a

IN BRIEF

Climate change is transforming the natural habitats of many species in ways that threaten their continued survival.

To save these organisms from extinction, conservationists are increasingly looking to move them to locations they have never occupied before.

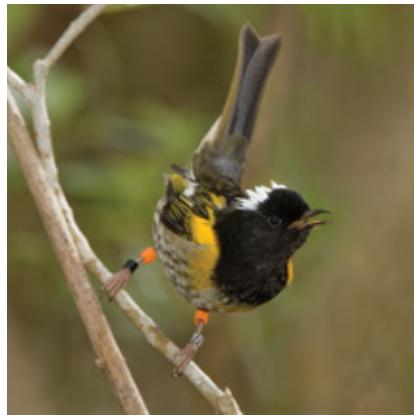
Such assisted colonization carries risks for both the relocated species and the destination habitats, but it may offer the best hope for preventing extinction.



MOUNTAIN PYGMY POSSUM

PROBLEM: The alpine habitat of this critically endangered Australian marsupial is warming so rapidly that the species cannot just shift its range uphill.

SOLUTION: Conservationists are currently debating where to move the nocturnal possum. The decision is complicated by the fact that they may need to also relocate its primary prey, the Bogong moth.



HIHI

PROBLEM: The hihi lives on and around New Zealand's North Island. Climate change in the coming years is set to render the area largely unsuitable for the bird.

SOLUTION: That shift will create favorable conditions for the hihi on the country's South Island, outside the historical range of the species. Conservationists are considering establishing a new population there.



KEY DEER

PROBLEM: Rising seas are poised to inundate large parts of the low-lying Florida Keys, where fewer than 1,000 of these tiny deer remain.

SOLUTION: Researchers have moved populations of key deer, a subspecies of white-tailed deer, to upland areas within the archipelago to buy them a few more decades of time.

new area. Conservationists elsewhere have also begun buying time in that fashion. In the Florida Keys, for instance, researchers have already relocated populations of key deer and the tree-like key cactus to upland areas to give them a few more decades of suitable habitat as sea levels rise. For Australia's Bramble Cay melomys, a small rodent, it is already too late for that kind of delaying tactic. In June, University of Queensland researchers announced that the species had vanished after repeated inundations of its island home. They described the event as probably "the first recorded mammalian extinction due to anthropogenic climate change."

Thus, the best hope for other species may lie beyond their traditional home range. For instance, the marshes where Australia's critically endangered western swamp tortoise lives outside Perth face the triple threat of climate change, urban expansion and the city's relentless drawing down of the underlying aquifer. Tracy Rout of the University of Queensland and her colleagues have used a supercomputer to sort through 13,000 potential relocation sites around the region. Further work on the ground has narrowed the list to several sites a few hours south of the city with hydrology and other conditions likely to remain suitable in the drier climate 30 to 50 years from now. After obtaining the necessary permissions from wildlife and environmental authorities, researchers drove south with a load of captive-reared tortoises this past August to begin introducing them to their new homes.

Other researchers are debating where to move Australia's critically endangered mountain pygmy possum. It is a measure of the complexity of such moves that they might also have to relocate its preferred food, the Bogong moth. The alpine habitat

for both species is warming so fast that simply moving uphill will no longer be possible.

The use of assisted colonization as a tool for tackling climate change is not entirely new. Stephen G. Willis, an ecologist at Durham University in England, and Jane K. Hill, now at the University of York in England, tried it experimentally beginning in 1999. "We had been looking at climate change impacts" on British butterfly species, including the relatively common marbled whites and small skippers, Hill says, "and we saw there was some suitable climate north of their normal range they hadn't reached."

The absence of the butterflies from that area stemmed from a phenomenon called migration lag. Even when natural corridors survive intact, species tend to lag behind the pace of climate change. That kind of delay might be predictable for trees, say. But studies have found that even birds and many mammal species lag behind shifts in climate, perhaps because they depend on slower-moving vegetation and habitat types. The gap between "climate velocity" and "biotic velocity" can be insuperable. For instance, Joshua J. Lawler of the University of Washington projects that as its rain-forest home becomes drier and warmer, South America's yellow-banded poison dart frog will need to hop hundreds of kilometers to the southwest to find suitable habitat later in this century.

When Willis and Hill noticed that marbled whites and small skipper butterflies were climate laggards, they set out to help them catch up. "We did it as a demonstration, as a good case study," Hill says. They were able to obtain the necessary permissions because the habitats for the proposed relocations were relatively restricted, in quarries and urbanized areas, and because other species there were already known to be compatible. They



WESTERN SWAMP TORTOISE

PROBLEM: Climate change and habitat destruction pose grave threats to this critically endangered Australian reptile, which dwells in wetlands outside Perth.

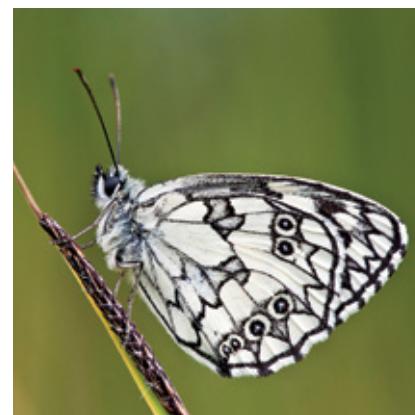
SOLUTION: Scientists have used a supercomputer to identify relocation sites for the tortoise that are likely to remain suitable decades from now.



YELLOW-BANDED POISON DART FROG

PROBLEM: Researchers project that as the species' rain-forest home in South America becomes drier and warmer, it will have to move hundreds of kilometers to the southwest.

SOLUTION: There is no known assisted colonization plan for this frog.



MARBLED WHITE

PROBLEM: Climate change is shifting the butterfly's habitat north, but the species has not followed suit on its own.

SOLUTION: Ecologists took marbled whites from North Yorkshire, England, and released them 65 kilometers north of the natural range of the species. The creatures appear to be thriving in the new locale.

released the marbled whites 65 kilometers north of their traditional range and the small skippers 35 kilometers north. Both populations seem to be thriving in their new homes, Willis reports. But he adds that the developing guidelines for assisted migration "are all saying the right thing: that you need to take a cautious, reserved approach. You don't want to be introducing the next rabbit into Australia."

TROUBLESHOOTING

TRANSLOCATING ANY SPECIES is inevitably fraught with risk. In a 2009 critique, Anthony Ricciardi of McGill University and Daniel Simberloff of the University of Tennessee, Knoxville, urged conservationists not to play "ecological roulette" and later warned that proponents have "grossly underestimated" just how difficult it is to forecast the impacts of introducing species to a habitat, even with the most cautious and nuanced analysis.

The two authors point to Newfoundland's 1960s decision to introduce red squirrels into its black spruce forests, with the idea that they would provide a new food source for the area's pine martens. The martens, weasel-like creatures then in decline, turned out to have no appetite for squirrels. The spruce cones, which had evolved squirrel-free for 9,000 years, had no means to protect themselves from the transplants. And the Newfoundland red crossbill, a bird subspecies that had evolved to depend on those same cones, collapsed in the face of new competition. The crossbill is now endangered and has become a case study of how the best intentions can go horribly wrong when people move species outside their historical range.

There may be ways to minimize the likelihood of such disastrous outcomes, however. Nathalie Pettorelli of the Zoological Society of London and her colleagues set out to do exactly that in a 2013 study of New Zealand's hihi, a beautiful bird with yel-

low and black plumage, hovering flight and 34 million years of evolution separating it from its nearest living relative. The bird survives in just five isolated habitats in and around the country's North Island, where conservationists provide support with the type of sugar feeders commonly used in North America for hummingbirds. Pettorelli and her co-authors found that climate change in the coming decades will make that northern habitat largely unsuitable for the hihi. On the other hand, the shift will open up appropriate habitat in South Island, outside the hihi's historical range.

"We were not looking to say when, or how, or where to move the hihi," Pettorelli recalls. That is the job of local managers. But the researchers thought they could provide a methodology for making such decisions carefully. They started by breaking out half a dozen separate ways things can go wrong for a translocation habitat—including negative effects on other species (ecological risk), introduction of new pathogens (disease risk), the possibility of spreading beyond the intended range and out-competing native species (invasive risk), hybridization with a related species (gene escape risk) and costs to human residents (socioeconomic risk). Then they considered a host of climate factors, such as how dry it gets in the dry season and how rainfall varies over the course of year, in old and potential new habitats, to make their models as precise as possible.

"We need to increase collaboration between people on the ground making the decision and the scientists," Pettorelli says. "A lot of people want to work together but don't know how to do it, don't have connections to work together." Even now "a lot of management decisions are taken without consideration of what science is available and how to make use of it." The point of the exercise was to show them how. As a result, conservationists are considering establishing a new hihi population on South Island.

UNCERTAIN OUTCOMES

AND YET EVEN PROONENTS of assisted colonization worry they may be getting ahead of themselves. Sometimes the “do no harm” option—leaving species to adapt on their own—can work out just fine. In the Rocky Mountains west of Denver, for instance, alpine flowers have become scarcer as temperatures have risen. So bumblebees that had evolved long tongues to specialize on flowers with deep pollen tubes have become less discriminating. That is reversing the evolutionary process, and the bees have lost a quarter of their tongue length over the past 40 years to feed on the flowers that are still there.

Species can also turn out to be resilient in ways scientists might not expect. In 2010 in southern Australia, researchers working on a commercial lobster fishery translocated 10,000 southern rock lobsters from deep water. But instead of moving them poleward to establish outpost populations in colder waters,

tuatara? Tuatara males can breed every year, whereas the North Brother females can produce a clutch of eggs only once every nine years. That means the females suffer constant mating harassment, which quickly erodes their ability to stay healthy—a problem that is worsening as the sex ratio of the species skews toward males. Because North Brother Island offers no shade and hardly any nooks and crannies to reduce the gender-skewing effect of warmer temperatures, the 500 or so tuatara there have become a bellwether for how a rapidly warming planet will affect the entire species. Already pushed off the mainland onto a handful of islands, the 100,000 or so remaining tuatara are the last survivors from 200 million years of evolution.

Nicola Mitchell of the University of Western Australia recently co-authored an article listing the various management options on North Brother. All the parties that care about the tuatara—scientists, government managers and the Maori, for whom

it is a cultural totem—could band together to remove unneeded structures and open up nesting sites on cooler faces of the islands. Or they could send in researchers to find eggs and use captive incubation to achieve the right temperatures for an equal gender mix. Alternatively, they could restore gender balance by protecting female hatchlings and adding them to the population while removing excess adult males.

“But these are all really difficult things to do,” says Mitchell, who spent two summers on the island searching for nests. “There are so few females nesting each year, and they’re very secretive and hard to find.” Relocating the tuatara to a cooler site might actually be a simpler solution, but it is expensive: every trip to North Brother Island involves a helicopter from downtown Wellington, a budget killer. Moreover, there are already insurance populations of the same subspecies (though a different genetic group) on other, nearby islands. The most pragmatic solution, then, may be to regard the North Brother Island tuatara as a sacrifice population. That is, scientists might just want to wait and watch how things work out on their own, and if the North Brother group crashes, so be it.

Ultimately such decisions will boil down to how comfortable conservation biologists and society as a whole feel about meddling with nature to decide which species survive and which die out. “When does it feel like you’re working with natural processes, and when does it feel like gardening?” University of Minnesota’s Hellman muses. “You can’t garden all of biodiversity.” ■

The developing guidelines for assisted migration “are all saying the right thing: that you need to take a cautious, reserved approach. You don’t want to be introducing the next rabbit into Australia.”

—STEPHEN G. WILLIS
Durham University

they moved them closer to the equator and inshore, to see how the species would handle the warmer conditions predicted in the near future. Counterintuitively, the lobsters went on to grow at four times the rate seen at their site of origin and to boost their output by 35,000 eggs a year. They were more adaptable to temperature changes than expected—and there was more to eat.

Predicting that kind of resilience is a challenge. When researchers recently examined how 155 species of British butterflies and moths fared over 40 years of climate change, they found that roughly half seemed to do better and half worse. Different factors mattered for different species, with some sensitive to summer temperatures, others to winter temperatures, some to spring rainfall, and so on, almost ad infinitum. “It turns out that these 155 different species of butterflies and moths have almost 155 different ‘opinions’ on how much the climate has changed and whether it has got better or worse,” observes Chris D. Thomas of the University of York.

So where does all this uncertainty leave a species like the tua-

MORE TO EXPLORE

Saving a Million Species: Extinction Risk from Climate Change. Edited by Lee Hannah. Island Press, 2011.

Biodiversity in a Changing Climate: Linking Science and Management in Conservation. Edited by Terry Louise Root, Kimberly R. Hall, Mark P. Herzog and Christine A. Howell. University of California Press, 2015.

FROM OUR ARCHIVES

Which Species Will Live? Michelle Nijhuis; August 2012.

RECOMMENDED

By Clara Moskowitz

MORE TO EXPLORE

FOR MORE RECOMMENDATIONS, VISIT

SCIENTIFICAMERICAN.COM/OCT2016/RECOMMENDED

Spaceman: An Astronaut's Unlikely Journey to Unlock the Secrets of the Universe

by Mike Massimino. Crown Archetype, 2016 (\$28)

The first astronaut to tweet from space was once a skinny kid from Long Island who dreamed of going into orbit. In his memoir, Massimino tells of how he ended up on the space shuttle 350 miles above Earth by way of getting a

Ph.D. in mechanical engineering, passing NASA's rigorous astronaut selection process and then being assigned to two Hubble Space Telescope repair missions—one of which provided the opportunity for his first trailblazing tweet. He shares the trials and joys of his time with NASA before his retirement in 2014; his insider's account of how the NASA community mourned following the 2003 *Columbia* shuttle disaster is particularly vivid. Massimino's narrative of becoming an astronaut is anchored by his honesty about his fear of failure and by his obvious affection for his fellow astronauts.

—Karl J. P. Smith

Cat Wars: The Devastating Consequences of a Cuddly Killer

by Peter P. Marra and Chris Santella. Princeton University Press, 2016 (\$24.95)

Outdoor cats kill roughly 2.4 billion birds a year in the U.S. alone, plus an additional 12.3 billion mammals and hundreds of millions of reptiles and amphibians. They are one of the greatest threats to wildlife in the country and are responsible for the extinction and decline of numerous bird species. Yet well-meaning cat lovers have consistently denied the evidence of cats' misdeeds and resisted efforts to combat the problem. For instance, they often advocate a process called "trap, neuter, return"—trapping feral cats, neutering and spaying them and then returning them to the wild—as a way to reduce the numbers of feral cats over the long term, even though studies have shown that the strategy can actually boost populations in feral colonies by drawing in unneutered animals. Marra, director of the Smithsonian Migratory Bird Center, and writer Santella make an impassioned plea for action in this compelling report on an often overlooked threat.

The War on Science: Who's Waging It, Why It Matters, What We Can Do about It

by Shawn Otto. Milkweed Editions, 2016 (\$20)



Writer Otto marshals an astonishingly broad range of facts, trends and history to make the case that "scientific advances in public health, biology and the environment are being resisted or rolled back." He examines the cultural and intellectual roots of current anti-science attitudes and concludes that a decades-long assault on science threatens democracy and civic progress in the U.S. and around the world. At times, Otto seems to be criticizing everyone—he eviscerates the ultraliberal antivaccine element and the "brutal, blame-the-victim aspect of New Age thinking." He reserves his greatest ire, however, for the "anti-science of those on the right—a coalition of fundamentalist churches and corporations largely in the resource extraction, petrochemical and agrochemical industries" that fight against evidence-based policy to protect destructive business models.

—Christine Gorman



ASTRONAUT Mike Massimino works on the Hubble Space Telescope during a 2009 space shuttle mission.

Why the Wheel Is Round: Muscles, Technology, and How We Make Things Move

by Steven Vogel. University of Chicago Press, 2016 (\$35)



If the wheel were square or oval or octagonal, it would never have become the most important technological innovation in human history—the device that makes possible not only efficient transportation but also gears, pulleys, motors and capstans (look them up). Vogel, who was an expert in both biomechanics and the history of technology, explains how it all unfolded, from the rolling logs that let our distant ancestors move heavy objects to such disparate inventions as the potter's wheel, the hurdy-gurdy and the yo-yo (the ancient Greeks played with them—who knew?). Vogel also answers the key question you never thought to ask: Although wheels can rotate indefinitely, our arms and legs, which operated the earliest wheeled machines, cannot, so how did our forebears bridge the gap? Read this truly engaging book to find out.

—Michael Lemonick

COURTESY OF NASA

I didn't talk
for a very long time

Jacob Sanchez

Diagnosed with autism

Lack of speech is a sign of autism. Learn the others at autismspeaks.org/signs.



AUTISM SPEAKS®



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

Methuselah's Moon Shot

Can science and Silicon Valley defeat death?

By Michael Shermer

Toward the end of his life, in an essay entitled “Topic of Cancer” in 2010 in *Vanity Fair*, Christopher Hitchens answered his own rhetorical query poignantly: “To the dumb question ‘Why me?’ the cosmos barely bothers to return the reply: Why not?”

The cosmos has never been particularly loquacious with its intentions, often requiring Brobdingnagian-sized ventures—from particle accelerators and space telescopes to genome and connectome projects—to tease out its deepest secrets. Can the same be done for death? A number of scientists and Silicon Valley billionaires think it can.



Oracle co-founder Larry Ellison, for example, has given more than \$430 million toward antiaging research because he finds the quiet acquiescence of mortality “incomprehensible.” XPRIZE entrepreneur Peter H. Diamandis co-founded Human Longevity, which, in conjunction with StartUp Health, launched the Longevity Moonshot, whose mission is “to extend and enhance healthy life by 50+ years and change the face of aging.”

Google co-founder Larry Page launched a biotech company called Calico, which aims to extend the human life span by a century. Calling it “a longer-term bet,” Page said he was confident they “can make good progress within reasonable timescales with the right goals and the right people.” One of those people is Ray Kurzweil, the scientist and futurist (and now a director of engineering at Google) who thinks that if we can survive until the 2040s, we can “live long enough to live forever.”

PayPal co-founder Peter Thiel created Breakout Labs to fund scientists and start-ups that include some working on achieving immortality, and he invested \$3.5 million in the Methuselah Foundation, co-founded by Aubrey de Grey, the biomedical gerontologist whose Strategies of Engineered Negligible Senescence (SENS) treats aging as an engineering problem to be solved at the cellular level by reprogramming cells to stop aging. A tireless promoter of the belief that our generation will be the first to achieve immortality—or at least to live indefinitely—de Grey is on record claiming that the first human to live 1,000 years is alive today. If you’ve seen any television show or documentary film on aging, you’ve seen the inimitable Aubrey de Grey, with his waist-length ponytail and Methuselahlike beard and baritone British accent. I’ve met Aubrey and shared a beer or two with him (if there is a fountain of youth in de Grey’s world, it bubbles with beer) as he leaned in to bend my ear on the latest shields against the grim reaper’s scythe.

I like beer, but I have my doubts. First, the second law of thermodynamics is paramount in the universe, so entropy will get us in the long run, if not the short. As the renowned astrophysicist Sir Arthur Stanley Eddington noted in 1928, “If your theory is found to be against the second law of thermodynamics I can give you no hope; there is nothing for it but to collapse in deepest humiliation.”

Second, extrapolating trend lines far into the future is problematic. Accelerating change may not continue at those rates nor apply to all technologies. Downsizing of computers from room size to pocket size is one thing; it is quite another to go from pocket size to cell size.

Third, according to a 2007 review paper in the journal *Clinical Interventions in Aging* entitled “The Aging Process and Potential Interventions to Extend Life Expectancy,” there is no single cause of aging and more than 300 theories for why cells deteriorate and stop dividing. The authors are thus led to conclude that “to date, no convincing evidence showing the administration of existing ‘anti-aging’ remedies can slow aging or increase longevity in humans is available.” And the SENS Research Foundation Web site admits: “No currently-available medical intervention or lifestyle choice has been shown to affect the basic human aging process.”

Still, hope springs eternal, and as Bill Gifford reported in last month’s *Scientific American* (“Living to 120”), there are some promising hints of antiaging properties of the diabetes drug metformin, which the FDA approved in 2015 for a clinical trial. If it helps more of us live healthy lives up to the ceiling of some 120 years, that would be welcome progress, but let’s not delude ourselves into believing radical life extension is around the corner. Our bodies are mortal, at least for now, but our genes are immortal as long as our species continues, so we owe it to future generations to create a sustainable planet and civilization. ■

JOIN THE CONVERSATION ONLINE

Visit *Scientific American* on Facebook and Twitter or send a letter to the editor: EDITORS@SCIAM.COM



Steve Mirsky has been writing the Anti Gravity column since a typical tectonic plate was about 35 inches from its current location. He also hosts the *Scientific American* podcast Science Talk.

Current Events

Boating through the Grand Canyon brings one face-to-wallface with geologic time

By Steve Mirsky

I'm afraid of a lot of things, but two things really terrify me: heights and turbulent water. So naturally I signed up for a white-water rafting trip in early July down the Colorado River in the Grand Canyon—including hikes in side canyons featuring some don't-look-down moments. I screwed up (keep reading) my courage because this trip was the annual canyon excursion organized by the National Center for Science Education.

Since 1981 the Oakland, Calif.-based NCSE has defended evolution education in public schools against constant threats from those who seek to remove it from biology curricula or to "balance" it with the addition of oxymoronic "scientific creationism" or its mutated progeny such as "intelligent design."

"So what does rafting down the Grand Canyon have to do with science education?" asked NCSE executive director Ann Reid, as we sat on driftwood at the Fern Glen campsite along the river on the penultimate day of our weeklong journey.

"Well, for NCSE it's one of the most powerful places on the earth to show the differences between religious thinking and scientific thinking," Reid observed. "The very small minority of Christians who believe the earth is 6,000 years old," she adds, see the Grand Canyon as "the best evidence they have of Noah's flood."

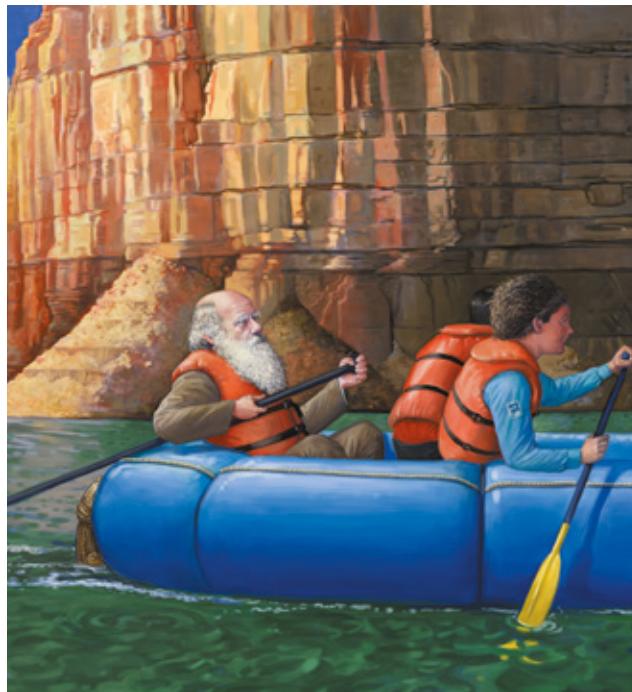
Creationists run multiple raft trips down the Colorado every year, during which patrons hear their take, including the notion that the inundation occurred some 4,400 years ago—and rapidly deposited the sediments of the canyon's walls.

"Of course, scientists of many different subdisciplines have figured out that the canyon is much older than that," Reid said of the perhaps still surprisingly geologically recent date of just five million to six million years ago. "There are the rocks, there's the biology, there's the hydrology—it's just a fantastic place to learn how scientists explain the world around us."

I'll talk more about some of the geologic history easily observable, even up close and at eye level, in the next issue. But now I want to tell you about living for a week in the Grand Canyon.

Our group of 25 traveled on what some disparagingly call "baloney boats," rafts some 35 feet long hugged on either side by huge inflated pontoons. Those would be the baloneys. If the crew of the *Pequod* had been on baloney boats, Ishmael might have wound up recounting a fairly mundane incident.

We nonetheless were told to hit the deck and hold tight to lashings when entering the most violent rapids. Because while the boat will float, a loose passenger could easily be thrown into the maelstrom, which is quite the bother and could result in all kinds of paperwork.



Late each afternoon we'd pull over and make camp. The key issue faced by the professional guides at that point was where to set up the two sanitation facilities. Urine goes directly into the fast-moving river, but solid waste gets collected all week and transported out. The metal collection devices are called groovers, allegedly because people out in the field would use empty steel ammo boxes for this purpose. Only they didn't have the luxury that we enjoyed: a seat. So the tops of the boxes' thin sides would leave a pair of temporary posterior indentations, aka butt grooves.

We performed our ablutions and laundry care in the river, which prompted one late-night visitation by the imaginary spirit of my great-grandmother, who berated me: "You bathe in river, wash clothes in river? We leave old country so you NOT have to go to river for bathing, clothes cleaning." When she found out that I actually paid to go on the trip, she became even more imaginarily livid: "Idiot." I'm just glad she didn't see my underwear hanging in a tree to dry overnight.

I came prepared for the searing heat, the burning sun, the frigid water. But what I couldn't have known was that my touch-screen Kindle would be useless at night. Because my headlamp (indispensable if you need the groover in the dark) attracted flying insects, which landed on the screen. And turned the page, changed the type size and might have purchased the complete works of Jean-Henri Fabre if we had any Internet connectivity. Fortunately, the remaining option was to turn the light off and look up from the river into a sea of stars. ■

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OCTOBER

1966 From DNA to Proteins

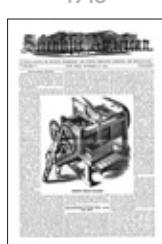
"The hypothesis that the genes of the living cell contain all the information needed for the cell to reproduce itself is now more than 50 years old. Implicit in the hypothesis is the idea that the genes bear in coded form the detailed specifications for the thousands of kinds of protein molecules the cell requires for its moment-to-moment existence: for extracting energy from molecules assimilated as food and for repairing itself as well as for replication. It is only within the past 15 years, however, that insight has been gained into the chemical nature of the genetic material and how its molecular structure can embody coded instructions that can be 'read' by the machinery in the cell responsible for synthesizing protein molecules.—Francis H. C. Crick"

In 1962 Crick had shared a Nobel Prize for his work on DNA.

Cold War Espionage

"Testimony by two scientists intimately involved in the wartime work at Los Alamos noted that the secret 'cross-section sketch' introduced in the espionage trial of Julius and Ethel Rosenberg and Morton Sobell in 1951 was worthless as a description of the bomb. The two scientists are Henry Linschitz, of Brandeis University, and Philip Morrison, of the Massachusetts Institute of Technology. On motion by Sobell, who is serving a 30-year sentence in Federal prison, the secret portion of the trial record has been opened to public inspection. Linschitz declared: 'It is not possible in any technologically useful way to condense the results of a two-billion-dollar development effort into a diagram, drawn by a high-school graduate machinist on a single sheet of paper.'"

In 2008 Sobell, at age 91, admitted turning over military information to the Soviet Union.



1866

1916 Warfare and Tanks

"The most novel, if not the most spectacular feature of the recent successful offensive by the French and British armies on the Somme, was the presence of several armed and armored tractors [see illustration], which, if we may judge from the press reports, proved wonderfully effective in following up the heavy gun attack. What part these machines are destined to play in the later stages of the war is a matter of pure speculation. The British speak of them as a great success; Berlin, naturally, describes them as being a complete failure—unwieldy, slow, and liable to break down."

Archive images on aspects of modern warfare in 1916 are at www.ScientificAmerican.com/oct2016/warfare

Power from the Sun

"It appears that although coal-fed steam boilers have been improved, sun boilers will be brought to a far better state of efficiency. This view is supported by recent experiments conducted at Meadi on the Nile River, 7 miles south of Cairo, during two years' work. The plant was

composed of five 205-foot boilers in the focus of five channel-shaped mirror reflectors, totaling an area of 13,269 square feet. The maximum quantity of steam produced was equal to 63 brake horse-power per acre of land occupied by the plant. These results seem to indicate the great value of solar boiler operation, especially where sunshine is plentiful and coal scarce."

1866 Grasshopper Scourge

"The Kansas farmers in Brown County and the adjacent territory appear to have been lately subjected to a plague similar to those inflicted on Pharaoh. The obstinate grasshoppers appeared in countless numbers, covering a track twelve miles in width, and consuming almost all vegetation. The Marysville *Enterprise* says: 'They alighted upon fields, gardens, fruit trees, and everything green or eatable, and, like a march of two hundred and fifty army corps, devoured every thing they touched. This whole country has been taken by them. Farmers are seriously alarmed lest the corn will be totally devoured.'"



1916: Imaginative depiction of a new wartime "tank," based on the scant public information available at the time.

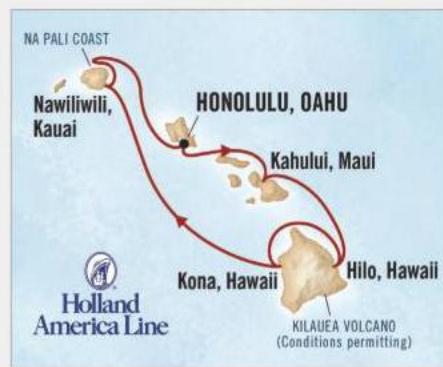
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SEMINARS

DINOSAURS

- The Paleobiology of Meat-eating Dinosaurs
- Alberta, Land of Dinosaurs
- What Killed the Dinosaurs?

SPEAKER:



**François Therrien,
Ph.D.**

Dr. François Therrien is the Curator of Dinosaur Palaeoecology at the Royal Tyrrell Museum of Palaeontology in Drumheller, Alberta. He holds a B.Sc. in Geology from the Université de Montréal, a Master's degree in Geosciences from the University of Rhode Island, and a Ph.D. in Functional Anatomy & Evolution from the Johns Hopkins University School of Medicine. Fresh out of his Ph.D., Dr. Therrien came to the Royal Tyrrell Museum as a NSERC postdoctoral fellow and was hired as a curator in 2006. Dr. Therrien's primary research interests focus on the study of faunal and environmental changes that occurred just before the extinction of the

dinosaurs as well as the study of dinosaur behavior, particularly that of extinct predators. Over the years, he has conducted field research in Canada, the USA, Romania, and Mongolia and has participated in numerous documentaries. In 2012, Dr. Therrien was involved in the discovery and study of the first feathered dinosaurs from North America.

HUBBLE AND KEPLER TELESCOPES

- Exploring the Milky Way with Hubble
- How the Universe Began
- The Search for Other Earths

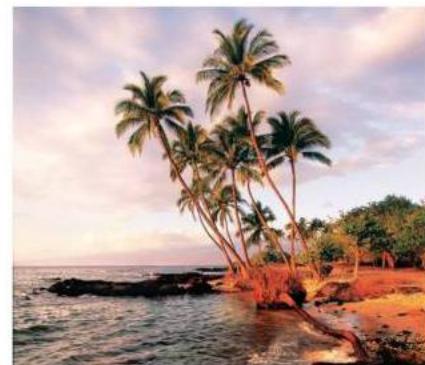
SPEAKER:



**David M. Meyer,
Ph.D.**

Dr. David M. Meyer is Professor of Physics and Astronomy and Director of Dearborn Observatory at Northwestern University. He received a B.S. degree in astrophysics (1980) at the University of Wisconsin and earned his M.A. (1981) and Ph.D. (1984) in astronomy at UCLA. Dr. Meyer's research

focuses on the composition, structure, and physical conditions of interstellar gas clouds in the Milky Way and other galaxies, and often makes use of observations obtained with the Hubble Space Telescope. At Northwestern, Dr. Meyer has specialized in designing and teaching introductory undergraduate courses in astronomy, cosmology, and astrobiology for non-science majors. His success in such efforts has led to a number of teaching awards including Northwestern's highest teaching honor — the McCormick Professorship of Teaching Excellence (in 2009). He has also developed and recorded two video courses for the Great Courses.



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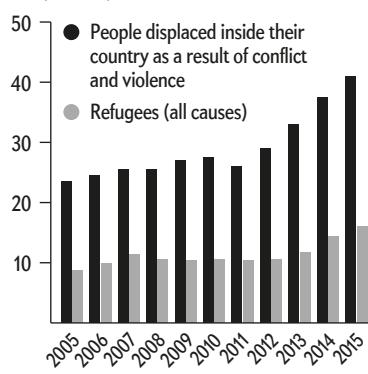
Pushed Out

Violence and disaster are increasingly forcing people to flee inside their own country

Every year millions of refugees abandon their native lands. But the number of internally displaced people—those who leave their home yet remain inside their nation—is even greater and is rising fast **A**. In 2015 alone, 28 million individuals were forced to make such a move **B**. Ironically, many countries will protect and assist refugees who cross into their territory but give no help to people who migrate internally in response to violence, natural and man-made disasters, or evolving crises such as drought. The migrants may live under terrible conditions for years. By highlighting this disturbing trend, international agencies hope that aid to them will improve.

—Mark Fischetti

A Cumulative Number of Migrants (millions)



B People Displaced inside Their Country in 2015

- Because of conflict
- Because of disaster
- Earthquakes, volcanoes
- Weather

In 2015 some 3.656 million people inside India were forced from their homes, more than in any other country. Two events caused much of the migration: massive flooding in November and a cyclone and flooding in July.

Conflict
8.8 million

Disaster
19.2 million

In the U.S., 63,000 individuals had to move internally, most because of flooding and wildfires.

10 Largest Displacement Events Total by Country or Region

406,000	Afghanistan
19,000	Algeria
36,000	Argentina
531,000	Bangladesh
11,000	Bolivia
59,000	Brazil
26,100	Burundi
82,000	Cameroun
13,000	Canada
211,100	Central African Rep.
36,000	Chad
1,047,000	Chile
3,602,000	Mainland China
228,600	Colombia
727,000	Dem. Rep. of the Congo
28,000	Dominican Rep.
78,100	Egypt
160,000	Ethiopia
34,000	Guinea
3,656,000	India
204,200	Indonesia
1,137,000	Iraq
486,000	Japan
19,000	Kazakhstan
105,000	Kenya
12,000	Laos
100,000	Libya
87,000	Madagascar
343,000	Malawi
21,000	Malaysia
97,000	Mexico
61,000	Mozambique
1,634,000	Myanmar
2,623,000	Nepal
85,000	Niger
837,000	Nigeria
1,002,000	Pakistan
171,000	Paraguay
2,509,000	Philippines
149,000	Somalia
214,000	South Sudan
66,000	Sri Lanka
152,300	Sudan
1,300,000	Syria
27,000	Taiwan
11,000	Tajikistan
942,000	Ukraine
63,000	U.S.
24,000	Uruguay
65,000	Vanuatu
45,000	Venezuela
10,700	West Bank
2,258,000	Yemen
	Other countries

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