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SCIENTIFIC AMERICAN

DAWN OF TECHNOLOGY

The discovery of 3.3-million-year-old stone tools overturns long-standing views on human evolution

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India's choices could have a profound impact PAGE 48

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ON THE COVER
Early human ancestor knaps stone tools, using an anvil and hammerstone to remove sharp flakes from a core. Archaeologists working in Kenya have uncovered stone tools dating to 3.3 million years ago—the oldest artifacts in the world. The discovery has upended conventional wisdom about the origins of our genus, *Homo*. Image by Jon Foster.

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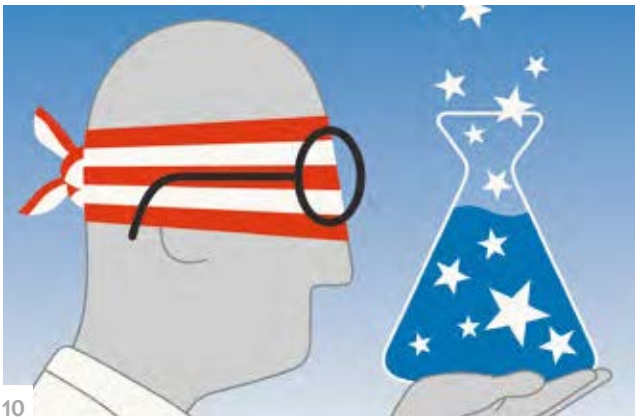

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ON THE WEB

The Eyes Never Lie
Richard Schwartz of the Graduate Center, City University of New York, uses eye-tracking technology to better understand children with specific language impairment (SLI). *Go to www.ScientificAmerican.com/may2017/sli*

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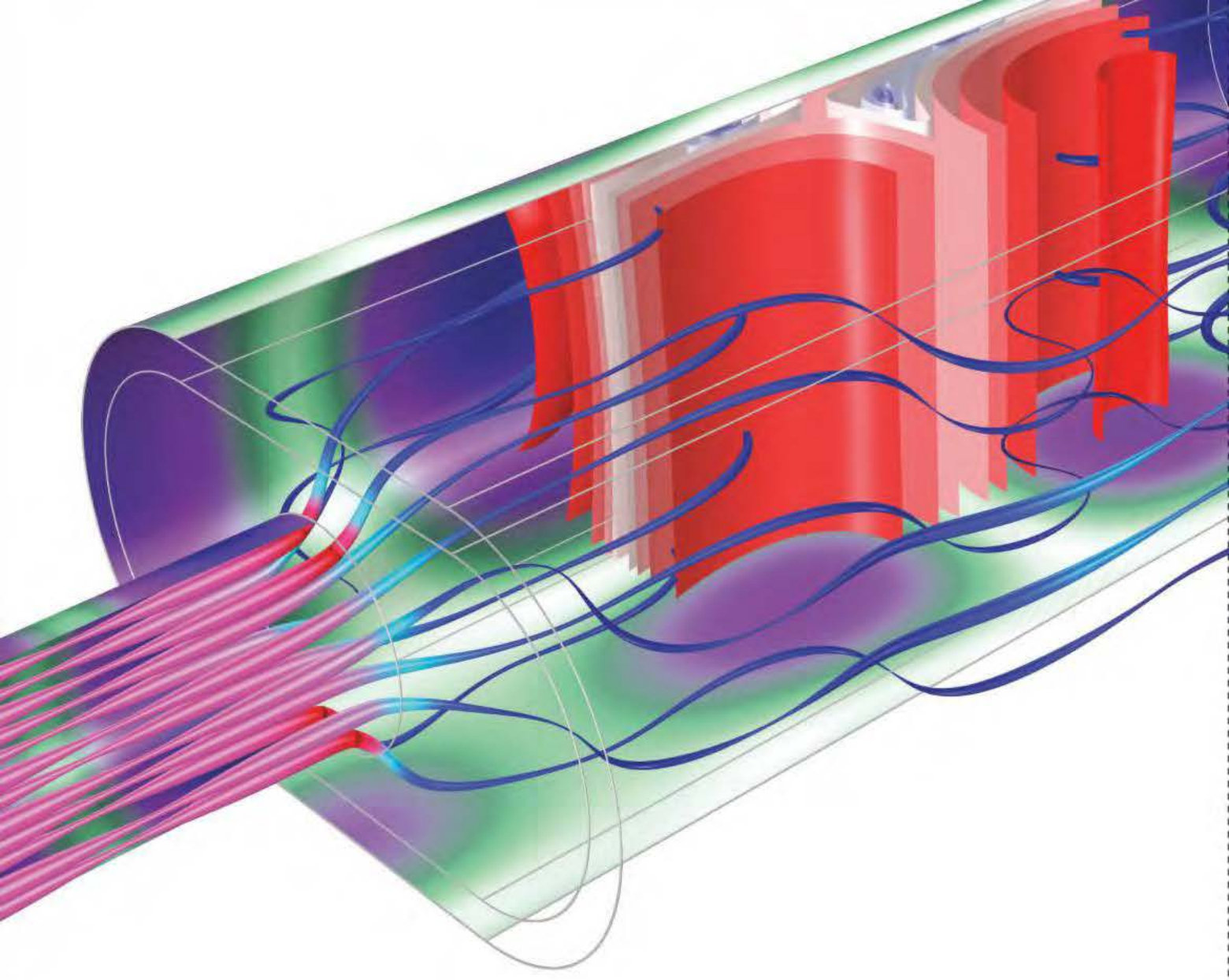


FROM THE EDITOR

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

Dawn of Innovation

A number of animals employ existing objects to carry out certain tasks. Seagulls drop mollusks onto rocks to crack open a snack, for example. Corvids wield twigs to create insect-gathering hooks. Apes probe termite mounds with sticks. But humans have taken tool use to a level no other creature has ever matched. Technology innovation is so extensive that Michael Haslam of the University of Oxford has said, "It's like an addition to our bodies."

In this issue's cover story, "The New Origins of Technology," starting on page 28, senior features editor Kate Wong investigates its surprisingly ancient beginnings. Recently Sonia Harmand and her husband, Jason Lewis, both at Stony Brook University, discovered 3.3-million-year-old tools at a site in Kenya called Lomekwi 3. The great age of the implements—far too early to be made by our own species, *Homo*—is forcing researchers to rethink what they believed they knew about the origins of technology and how incorporating tools into our existence has, in turn, shaped the human family tree.

Could alien technology be causing the mysterious dimming of Boyajian's star, also known as KIC 8462852, more than 1,000 light-years away from Earth? Probably not, write Kimberly Cartier and Jason T. Wright in their feature, "Strange News from Another Star." Still, the two astronomers are among those who find it difficult to account for the dramatic and sporadic dimming with natural phenomena. Theorists posit exotic possible explanations, among them comet swarms or black holes. Beyond those is the intriguing possibility of an advanced cosmic civilization. Sound far-fetched? Turn to page 36 to learn more.

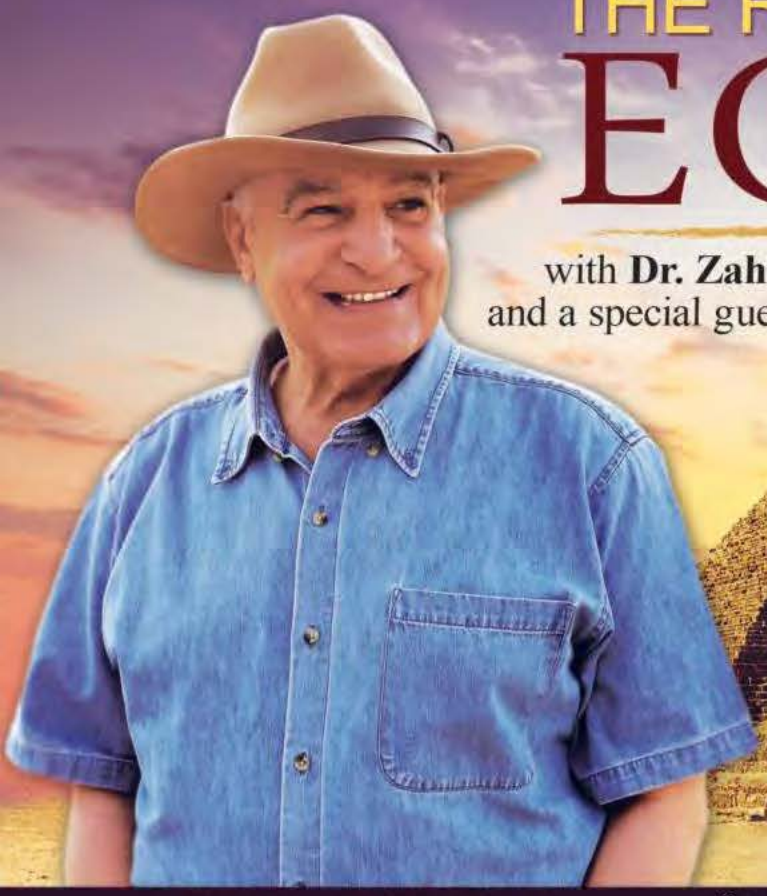
Technology has its downsides, of course. Thousands of studies demonstrate that human activity, including the burning of fossil fuels, has led to global climate change. But how bad will it be? That's a question that will depend at least in part on the actions of a number of major emitters.

In "The Global Warming Wild Card," starting on page 48, Varun Sivaram, a fellow at the Council on Foreign Relations and acting director of its program on Energy Security and Climate Change, examines one wild-card country in our climate future: India. With its population and living standards rising quickly, India could prevent the world from limiting global warming to sought-for levels—or it could help make the difference in a better future. It is already the third-largest emitter after China and the U.S. but could become the largest by midcentury if it does not take strong measures. Can India make a low-carbon transition? Technical and financial support from other nations will be crucial. SA

Illustration by Nick Higgins

THE ROYAL TOUR TO EGYPT

with **Dr. Zahi Hawass**, the legendary archaeologist
and a special guest **Mrs. Jehan Sadat**, Egypt's First Lady



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Mrs. Jehan Sadat

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January 2017

LIFESAVING VESSELS

"Heart Therapy," by Gabor Rubanyi, explains how the heart can develop new blood vessels in response to blockages in the coronary arteries (although it does not do so enough to get around the blockages for most patients). It also describes investigations into how to promote these so-called collateral vessels.

The article answers a question I have had for 28 years. Until my first, minor heart attack in 1989, I had been running four miles, five days a week for more than a decade. Then, suddenly, I was unable to run at all. My doctor, knowing my family health history, suspected trouble, and he was right. It was pretty exciting for the cardiology staff examining me when I experienced a second heart attack while I was hooked up to an electrocardiogram on a treadmill. I simply became very exhausted.

After undergoing a double-bypass surgery, which was a breeze at age 43, I went home and mowed the lawn. I asked the surgeon about muscle damage, and he indicated that the area was about 10 millimeters across even though one of my coronary arteries was completely blocked and had been for a very long time. He also said that my collateral circulation was highly developed.

I had always wondered what was primarily responsible for this circulatory savior. The possibilities were vigorous exercise or natural processes. Rubanyi makes it clear that both were contributors. Hence, I can thank my usually terrible, but here lucky, genes and my exercise program.

FRED BROWN
Dallas, Ore.

"It is important to lay out forecasts and policy responses for the reality of AI displacing not just blue-collar labor but also highly skilled professional work."

BRIAN J. TURNER *GERRARDSTOWN, W.V.*

DANGERS OF AI

Scientific American should offer a counterbalance to the complacency of Gordon Briggs and Matthias Scheutz's assertion that "superintelligent machines that pose an existential threat to humanity are the least of our worries" ["The Case for Robot Disobedience"] (echoed in Michael Shermer's casually dismissive "Apocalypse AI" [Skeptic] in the March issue). While the benefits of technology's expanding reach are abundant, many serious thinkers—including Stephen Hawking, Elon Musk and Bill Gates—have expressed fundamental concerns about the possibility that machines could come to exceed human capacity for thinking.

Scientific American has a broader role than cheerleading for new science and technology. It would be feasible for it to organize leading analyses addressing potential longer-range catastrophic changes, such as the "singularity": when machine intelligence exceeds human intelligence. It would also be important to lay out forecasts and policy responses for the already current reality of AI displacing not just "mundane" blue-collar labor but also highly skilled professional work, such as medical diagnoses or legal research. Our society seems to be turning a corner where overblown concerns about the job threat of automation from the 1950s have morphed into a broader and very real challenge—one that requires a greatly expanded approach to retraining adult workers and updating education to support lifetime flexibility across occupations.

BRIAN J. TURNER
Gerrardstown, W.V.

FACT-DEFLECTING

In "When Facts Backfire" [Skeptic], Michael Shermer discusses cognitive dissonance—in which holding two incongruous thoughts at the same time creates an uncomfortable tension, prompting people to spin-doctor facts to reduce it—and the backfire effect—in which corrections to an erroneous idea that conflict with a person's worldview or self-concept cause that person to embrace the error even more.

What would be the evolutionary advantages that would cause us to develop these two brain attributes? In our current time, I can see only the disadvantages.

WILLIAM BLACK
Earleton, Fla.

SHERMER REPLIES: First, the backfire effect is just a description of an observation of what people do in response to facts counter to their beliefs, not a brain attribute. Cognitive dissonance is a better descriptor for an internal state, although we should remember that all such descriptions are inferences from behavior, language, brain scans, and so on, not direct observations of someone else's mind.

Second, there are good reasons to think that cognitive dissonance has an evolutionarily adaptive purpose, as social psychologist Carol Tavris outlined it in an e-mail to me: "When you find any cognitive mechanism that appears to be universal—such as the ease of creating 'us-them' dichotomies, ethnocentrism ('my group is best') or prejudice—it seems likely that it has an adaptive purpose. In these examples, binding us to our tribe would be the biggest benefit. In the case of cognitive dissonance, the benefit is functional: the ability to reduce dissonance is what lets us sleep at night and maintain our behavior, secure that our beliefs, decisions and actions are the right ones.

"The fact that people who cannot reduce dissonance usually suffer mightily (whether over a small but dumb decision

or because of serious harm inflicted on others) is itself evidence of how important the ability to reduce it is."

HOSPITAL SECURITY

In "Keep Hospitals Weapons-Free" [Forum], Nathaniel P. Morris argues that "Tasers and guns issued to security guards" at hospitals "do more harm than good." I worked in security at a zoo for a decade or so, and we carried only pepper spray. But given the concern of animals potentially escaping, we kept a few shotguns in locked cases in various locations around the zoo. Perhaps something like that approach could work in hospitals as well.

Scott Isler
via e-mail

MODEL MUSINGS

There is a clear connection between Clara Moskowitz's article about an investigation of whether space and time could be made of tiny informational building blocks ["Tangled Up in Spacetime"] and Juergen A. Knoblich's article on growing part of the developing human brain in the lab for research ["Lab-Built Brains"]. In both cases, scientists are trying to stimulate insight by constructing "toy models" of something out there in the real world (the universe in one case, the brain in the other).

Of course, in the case of spacetime, the model is a theory, whereas in the case of the brain, the model is a so-called organoid that enjoys its own existence. Yet the two are not that different. Applying the holographic principle that Moskowitz describes—in which certain physical theories may be equivalent to ones applicable to a lower-dimensional universe—we could say that one kind of conception is a 2-D version of the other. The question remains, however, of which is which.

Jack Petranker
Director, Center for Creative Inquiry
Berkeley, Calif.

CLARIFICATION

"Data Deliver in the Clutch," by Steve Mirsky [Anti Gravity], refers to Daniel Kahneman as a Nobel economist. His field is primarily psychology, but he shared the 2002 economics Nobel Prize for his work in behavioral economics.

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A March for Science Is Not Enough

To fight antiresearch policies, scientists must become activists for the long haul

By the Editors

Earlier this year scientists announced that on April 22—Earth Day—they intended to, in their own words, "walk out of the lab and into the streets." Organizers of this March for Science were dismayed by a new administration and a Congress pushing policies likely to increase pollution, harm health, reduce our ability to forecast natural hazards such as hurricanes—and toss accepted science out the window. The protests, planned for Washington, D.C., and other cities around the U.S. and the globe, quickly gathered support from major scientific societies, tens of thousands of volunteers, hordes of Twitter supporters and 800,000 members in a Facebook group.

It's a start—but not enough to make a lasting impression on the president, Congress or state legislators.

"Don't tweet at them. Don't sign goofy-ass useless internet petitions. Call," tweeted David Shiffman, a marine biologist at the University of Miami. He is right. People need to reach out individually to members of the government and make it clear that they will back their opinions with votes.

Protest marches can be effective. The civil-rights demonstrations in the 1950s and 1960s showed politicians that a huge number of people opposed prejudice and segregation and were willing to take action. The March for Science could do the same thing. Rush Holt, chief executive officer of the American Association for the Advancement of Science—and a former U.S. representative for New Jersey as well as a physicist—said that his organization supported the march because President Donald Trump's election has triggered many attacks on evidence and rational thought as guides to national policy. He was also alarmed by politically based attacks on the integrity of the scientific enterprise. There are concerns that Trump supporters and conservative politicians will dismiss the march as nothing more than the whining of elites. As a result, some scientists were reluctant to get involved—but many others were all in.

There are ways, however, to make sure the marchers' message will linger in politicians' minds after the crowds disperse. Scientists can run for office themselves, and a new group called 314 Action, named for the first three digits of pi, is recruiting. Funded by some 80,000 donors (as of March), 314 Action, co-founded by Shaughnessy Naughton, a chemist, will give both money and political training to scientist-politicians. Naughton has enlisted the help of political campaign strategist Joe Trippi, who has guided several Democratic candidates into congressional seats.

Running for office is, in many ways, an unscientific endeavor. Campaigns are not controlled experiments, and rough-and-tumble real-world politics can be an uncomfortable new experience. But Kate Knuth, an environmental scientist who served several terms in the Minnesota House of Representatives, told the *Atlantic* that she learned invaluable lessons knocking on strangers' doors and asking for their votes. "I never felt like I knew more about how people were thinking about the problems in their community, what they wanted from government, and their hopes and dreams for the future," Knuth said.

Those who do not run can vote and let politicians know that votes, like science, will follow the evidence. People can call state or federal representatives and say that if they do not act to support—to pick one example—the National Oceanic and Atmospheric Administration's offices that predict storm severity or coastal erosion, representatives will lose at the ballot box. Scientists and ordinary citizens can also donate money and time to groups that advocate for government policies that are backed by scientific and medical facts.

It's the kind of response that goes on far longer than a march. SA

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Illustration by Celia Krampien

The War on Facts Undermines Democracy

Politicians must not interfere with the free and open pursuit of science

By Jonathan Foley

Jonathan Foley is executive director of the California Academy of Sciences in San Francisco. He serves on *Scientific American*'s board of advisers.

Scientists around the country are nervous as hell. There seems to be a seismic shift happening in Washington, D.C., and our government's relationship with facts, scientific reality and objective truth has never been more strained.

It started with "alternative facts" about the size of the crowd at Donald Trump's inauguration. The White House also asserted, without any evidence, that widespread voter fraud cost Trump the popular vote, even though numerous, bipartisan sources have debunked that claim. My parents' generation would have called such alternative facts falsehoods or even lies. It is not just the peddling of conspiracy theories that is troubling, however. Worse still is that the White House and many members of Congress seem opposed to the very *pursuit* of facts and have tried to place draconian restrictions on what federal scientists can research, publish or even discuss. And who knows what will happen to our nation's long-standing investments in research and science education?

Science shows us the magnificence of our world. Our oceans hold beautiful coral reefs, bursting with life, gleaming through azure waters. Tropical rain forests teem with creatures, sights and sounds. Here in California we have giant redwoods, reaching skyward, drenched in mist. And off our shores, there are colossal whales, drifting in rich waters, raising their young and singing their ethereal songs.

Through the lens of science, these wonders stir the mind. They awaken our hearts and souls. We instinctively want to share them with the people we love, and preserving them is the greatest gift we can give our children. But science also tells us that these wonders are at risk from widespread habitat loss, pollution and climate change. Science shows us the planet is in trouble, even if many politicians ignore the evidence.

All is not lost, however. Science shows us ways to build a sustainable future—by reinventing our energy system, agriculture and cities. Science can build a future where people and nature thrive together, for generations to come. Ignoring science will doom us to an impoverished, degraded world. Our children deserve better than that, and only science points the way forward.

Ultimately a healthy democracy depends on science. When Congress asked physicist Robert Wilson in 1969 what a new particle accelerator would do to help with national defense, he answered that it would do nothing. The pursuit of scientific truth, he said, "only has to do with the respect with which we regard one another, the dignity of men, our love of culture." The pursuit of truth, an informed citizenry and the unfettered exchange of ideas are cornerstones of our democracy. They are what make America great. Rejecting evidence and empiricism is a step toward despotism.

There is a long tradition of bipartisan support for science and an evidence-based worldview in the U.S. In fact, the Union of Concerned Scientists has ranked presidents from both parties as exceptional supporters of science, including Abraham Lincoln, Teddy Roosevelt, Harry S. Truman, Richard M. Nixon, Jimmy Carter and George H. W. Bush. Wise leaders have almost always recognized the value of independent science to our democracy.

There is something different about the Trump administration. Something troubling, which scientists need to stand up and call out. While we generally avoid political conversations, scientists should always defend facts, objectivity, and scientific independence and integrity. Not doing so would be almost unethical. So to the Trump administration, I would say this: If your apparent disregard for facts is just a series of missteps, so be it. Say so. Fix it. It would be brave. It would be wise. And it would show some class.

But if this is actually part of your governing philosophy, I would give you a warning on behalf of my fellow scientists: Do not mess with us. Do not try to bury the truth. Do not interfere with the free and open pursuit of science. You do so not only at your peril but also at the peril of the nation. SA

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Illustration by Thomas Fuchs

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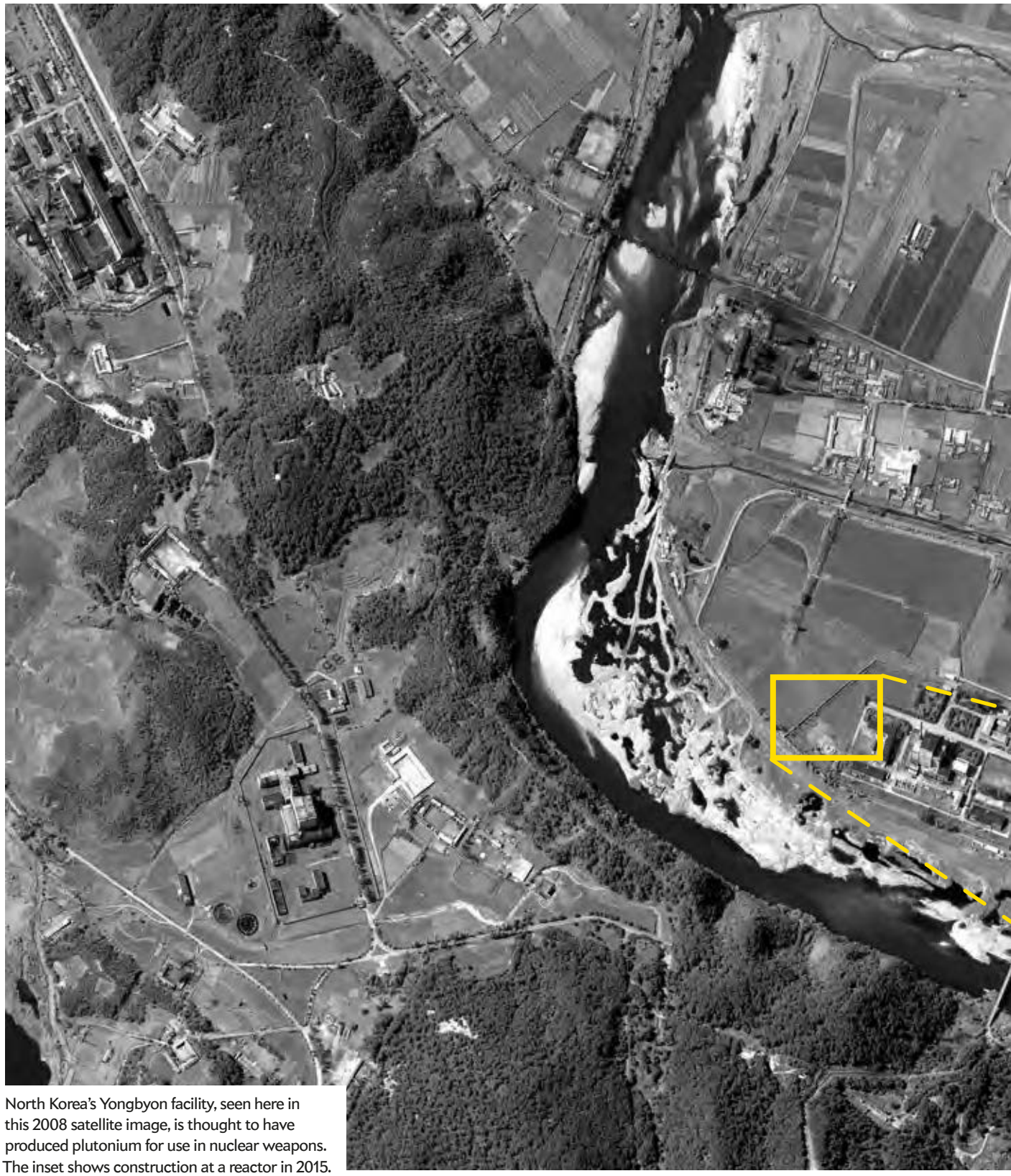


North Korea's Yongbyon facility, seen here in this 2008 satellite image, is thought to have produced plutonium for use in nuclear weapons. The inset shows construction at a reactor in 2015.

INSIDE

POLICY

Nuclear Ghosts

A new project could detect concealed weapons programs

The year is 2030. After years of wrangling, the North Korean leadership agrees to stop making weapons-grade plutonium and to destroy its stockpiles. Officials invite inspectors to watch them load this nuclear fuel into reactors and transform it into a form useless for bombs. Yet the North Koreans secretly divert some plutonium and fill the reactor instead with lower-grade uranium. The uranium emits radiation, including neutrinos and their antimatter counterparts, antineutrinos—harmless and light subatomic particles that pass ghostlike even through lead or rock. Suspecting a ruse, the international authorities park an SUV-sized device near the North Korean reactor. Within months they confirm the deception via a telling pattern of antineutrinos streaming from the facility.

That scenario could become reality in coming years as tools of particle physics are used to combat illicit nuclear programs. A new proposal, detailed recently on the preprint server arXiv.org, describes how to build an antineutrino detector that could, over the course of a few months, determine if weapons-grade fuel is being used in a reactor. The need for such detection methods has become more urgent. North Korea has advanced its missile technology, and Iran has developed the capacity for its own nuclear weapons program, making verification a key issue. In March, Secretary of State Rex Tillerson called for a "different approach" to sty-

mieing North Korea's nuclear aspirations, saying that diplomatic pressure alone had failed.

Antineutrinos are a by-product of the fission in a nuclear reactor, in which an atomic nucleus of a radioactive element such as plutonium splits into lighter elements. One type of radioactivity, called beta decay, releases either a positron and a neutrino or an electron and an antineutrino. That antineutrino is the "tell" for a reactor because only the radioactive elements in nuclear fuel emit lots of them at a steady rate.

Antineutrino-based nuclear surveillance is the impetus for a U.S.-led project called WATCHMAN (for WATer CHerenkov Monitor for ANtineutrinos). A WATCHMAN device would consist of a tank containing thousands of tons of gadolinium-doped water and could theoretically detect antineutrinos from an illicit reactor up to 1,000 kilometers away. It is hard to diplomatically ask a wary nation to let inspectors build giant water tanks close to heavily guarded facilities, so such detection distances are handy.

When an antineutrino hits a proton—a hydrogen nucleus in a water molecule in the giant tank—it transforms that proton into a neutron and a positron. The positron moves so fast that it emits light called Cherenkov radiation, the optical equivalent of a sonic boom produced when a charged particle moves faster than the speed of light through some substance. Nothing goes faster than light moving through a vacuum, but in another medium—such as water, glass or air—light moves slower and can be outpaced. Thus, a positron from an antineutrino will create a flash of light in a WATCHMAN tank. Meanwhile the gadolinium in the water will sop up the neutron, a process that emits a second flash. This characteristic double flash reveals the presence and direction of a nuclear reactor.

WATCHMAN can indicate whether a reactor is active and where it is but not the precise mix of fuel, such as highly enriched plutonium and uranium. Patrick Jaffke, a postdoctoral researcher at Los Alamos National Laboratory and co-author of the new proposal, suggests a small version that could be placed close to a reactor to determine the type of nuclear fuel within by analyzing the activity of antineutrinos. His design would measure the spectrum and shape of the initial Cherenkov flash and thus the energy of the progenitor antineutrinos from the positrons. By charting the energy distribution of the detected positrons, an inspector could estimate how much of the total antineutrino emission was from a given fuel type in a reactor's core.

Instead of water, Jaffke suggests using plastic or another proton-packed hydrocarbon to boost the chances for antineutrino collisions and to reduce a device's size by orders of magnitude. Such a detector could then be placed within dozens of meters of a reactor.

Although such a detector would be smaller, there would still be the issue of background noise. Cosmic rays, for example, can create neutrons that look similar to ones from neutrino reactions. Putting the antineutrino detector five to 10 meters underground and fairly close to a reactor might solve this problem, says Steven Dazeley of Lawrence Livermore National Laboratory, who led a 2016 analysis of noise issues facing WATCHMAN. Additional shielding around the device could also help.

There are other ideas for devices that need little or no shielding. And help could come from several groups around the world working on neutrino- and antineutrino-detection technologies for physics research.

"There's been a longtime search for a practical use of antineutrinos," Jaffke says. "That's one of the coolest aspects" of using the particles to detect weapons-grade nuclear fuel. Let's hope it doesn't find any.

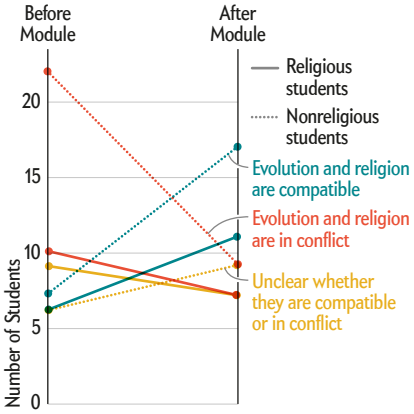
—Jesse Emspak

EDUCATION

Dissent with Modification

Acknowledging students' religiosity could increase acceptance of evolution

On topics ranging from astrophysics to public health, rejections of scientific consensus can prove quite inflexible when bolstered by religious doctrine. But a new approach to teaching evolutionary biology appears to ease such tensions. It involves airing perceived conflicts between religion and evolution in the classroom rather than simply presenting a mountain of evidence for evolution. Such a curriculum could help biologists (most of whom claim to hold no religious beliefs) more effectively prepare students (most of whom profess belief in God) to meet the nation's growing need for scientists and technologists.



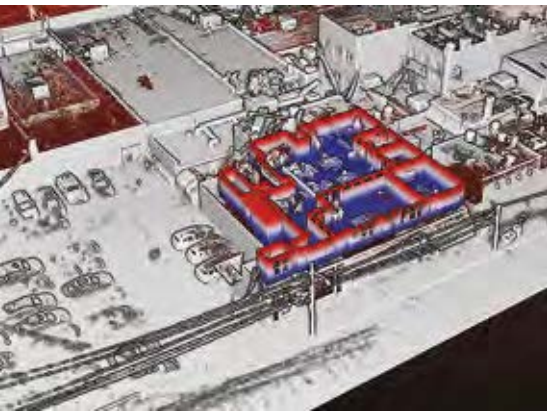
During a two-week module on evolution that was part of an introductory biology course at Arizona State University, the instructor explored a variety of viewpoints about the relation between some religious beliefs and the development and diversification of life, ranging from evolution without the involvement of a deity to various types of creationism—including theistic evolution. Students were encouraged to express their opinions and concerns.

Surveys filled out by 60 students before and after the module revealed that the number of students who perceived a sense of a conflict between religion and evolution at the start was cut in half by the end. An analysis of the results is detailed in the February issue of the *American Biology Teacher.*

In response to instructors' concerns about limited classroom time, a follow-up project compressed the two-week module to six minutes. Remarkably, unpublished results suggest this brief exposure also proved effective at reducing students' perception of a conflict. "If we encourage national policy documents that promote these teaching practices," says study co-author Elizabeth Barnes of Arizona State, "perhaps we can increase acceptance of evolution among our students, future teachers and future political leaders." *—Robin Lloyd*

PRECEDING PAGES: DIGITALGLOBE *Getty Images;* THIS PAGE SOURCE: "IMPACT OF A SHORT EVOLUTION MODULE ON STUDENTS' PERCEIVED CONFLICT BETWEEN RELIGION AND EVOLUTION," BY M. ELIZABETH BARNES ET AL., IN *AMERICAN BIOLOGY TEACHER*, VOL. 79, NO. 2, FEBRUARY 2017

Graphic by Amanda Montañez



A 3-D map of the interior of these commercial offices can be modeled in less than half an hour, makers of a new device say.

COURTESY OF KAARTA

GEOGRAPHY

Maps on the Move

A portable laser range finder could help builders go digital

Major automakers—along with upstarts such as Tesla and Uber—are racing to put self-driving cars on the road, leading to advances in enabling technologies such as laser range finders known as lidars. A lidar works like a hyperactive laser measure, scattering laser light in multiple directions to gather hundreds of thousands of measurements per second and build up a "point cloud" of spatial information. A computer processes these data to form a coherent picture of a vehicle's surroundings.

Now a Pittsburgh-based start-up called Kaarta has integrated a lidar—more affordable and speedier these days, thanks to accelerated development by suppliers serving the auto industry—with a motion sensor, processor and seven-inch touch screen into a handheld device. Called the Contour, the device enables architects, builders and others to generate 3-D computer models of their surroundings on the fly as they walk through them, the company says. A camera on the device captures color data and maps them onto point clouds to render models in realistic hues. When loaded into standard computer-aided design (CAD) software, the models can then form the basis of building renovation plans or other projects.

The Contour moves well beyond the measuring-tape-and-clipboard approach most builders still use to get data for CAD models, Kaarta CEO Kevin Dowling says, and that will save time. The company expects to start shipping devices to customers by the second half of 2017. —*Michael Belfiore*

1

2

Dome-shaped nest of a small ground finch (*Geospiza fuliginosa*) (*1*); cup-shaped nest of a chipping sparrow (*Spizella passerina*) (*2*).

SHARON BEALS

EVOLUTION

Home Sweet Dome

Nest-building behavior started with birds making spherical domes

Which came first, the cup or the dome? Unlike the old chicken-versus-egg conundrum, this question appears to have an answer. A new study suggests that the familiar open-cup style—built by nearly three fourths of today's passerines, or perching birds—is a modification of roofed spherical structures that just a handful of species now make.

Most biologists had theorized that nest shape evolved the other way around, from bowl to dome. Researchers recently tested the hypothesis by overlaying nest-structure data on three different phylogenetic trees, thought to represent the evolutionary relations among 281 Australian passerine species. The team noticed that species with particularly ancient lineages, such as lyrebirds, scrub-birds and New Zealand wrens, still build roofed structures—suggesting that ancestral passerine nests were domed. A statistical analysis of the likelihood that particular nest shapes occurred in ancestors confirmed the hunch: the dome came first.

The researchers also found that making cup-shaped nests evolved multiple times and in different lineages; 187 of the studied species build them today. The results were detailed in February in the *Proceedings of the Royal Society B.*

Cups may offer some advantages, such as being easier to build or to abandon if predators approach. "I think most people had assumed that roofed nests evolved from cups, in part because roofed nests are so unusual today," says co-author J. Jordan Price, a professor of biology at St. Mary's College of Maryland. "This nicely illustrates how the current prevalence of a trait, such as cup nests, does not necessarily indicate the order of events during its evolutionary history."

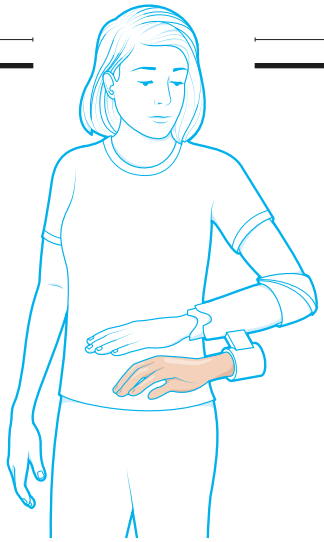
The findings could inform how scientists study nest evolution, says Gavin Leighton, an evolutionary biologist at the Cornell Lab of Ornithology, who was not involved in the study. "I think there will be increased interest in determining the ecological scenarios that select for different nest types," he says. Seems you can't put all your nests in one basket.

—Kat Long

MEDICINE

A Spare Hand

People with nerve-damaged hands can now have them surgically replaced



Some 1.6 million people in the U.S. live with limb loss, according to a 2008 study, and that number could more than double by 2050. Modern prostheses enable replacements of limbs lost to injury or disease. But people who lose functionality in an otherwise healthy arm or leg have had few options. A team of surgeons in Vienna, Austria, however, recently developed bionic reconstructions of the hands of 16 people who had lost manual control and sensation because of nerve damage. The catch: patients have to undergo a nonessential amputation of the damaged hand to make room for the prosthesis.

Hoping to clarify the choices and considerations, surgeon Laura Hruby and her colleagues at the Medical University of Vienna in Austria published a protocol for selecting the first patients to undergo this intensive procedure and guiding them through it.

The Vienna team focused on people with damage to the brachial plexus, the cluster of nerves that controls muscles in the shoulders, arms and hands. "Bionic hand reconstruction in patients with brachial plexus lesions, in whom classic primary and secondary reconstructions have failed, gives hope to patients who have lived without hand function for years or even decades," Hruby says.

The approach improved hand dexterity beyond what would be possible with surgical intervention, according to the research, which was published online in January in the *Journal of Neurosurgery*. It also reduced the severe, spontaneous pain that can develop in limbs that sustain nerve damage. —*Dan Robitzski*

Steps toward Reconstruction

1. Bionic hands are mounted adjacent to the original hand onto an arm brace and wired to electrodes that can pick up the candidate's functional forearm nerves through the skin. This stage gives people practice controlling the prosthesis.

2. The original hand is surgically removed.

3. After recovery from surgery, the bionic hand is moved from its temporary position on the arm brace to the end of the candidate's wrist.

Illustration by Brown Bird Design

EARTH SCIENCES

Soil in the Forecast

New landslide-prediction models could enable lifesaving and trustworthy alerts

For several days in late September 2015, heavy rains soaked the earth surrounding the district of El Cambray II in Guatemala. On the first night of the following month, steep slopes, long held in place by thick, tropical tree roots, suddenly gave way, burying hundreds of homes in mud up to 15 meters deep. At least 280 people died.

Officials had warned residents for years that the area was at risk, but a mixture of poverty and mistrust leads some of the poorest people in Central America and beyond to build and live on marginal land. Still, residents of El Cambray II might have been willing to temporarily evacuate, if they had received a credible and precise warning. And if such warnings were available worldwide, they could help reduce the 3,000 deaths attributed to landslides every year.

Fortunately, slide alerts worth heeding are in the works—and the El Cambray II event gave scientists their first new landslide data against which to validate a novel software system for monitoring the hazards in near real time. The basis is U.S. National Oceanic and Atmospheric Administration infrared and microwave satellite data, which enable a global forecast of rainfall at a four-kilometer resolution for up to six hours into the future. Scientists at the Hydrologic Research Center (HRC) in San Diego, who developed the system, add local weather radar and rain-gauge data where available to help predict likely flash floods. A new component for predicting landslides integrates global soil-moisture assessments. In Guatemala, local partners combine all these data onto a digital map of more than 8,000 known historic landslide sites to yield risk estimates as frequently as every six hours. The resulting landslide warnings focus on the effects of a specific storm on areas just two to four kilometers across. Such alerts are harder to ignore than blanket warnings, which might be in place for days or cover entire valleys, and may not account for local soil conditions.

1

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The aftermath of the disaster at El Cambray II, as it appeared on October 2, 2015, just outside Guatemala City (*1*). Rescuers searching the following day for victims (*2*).

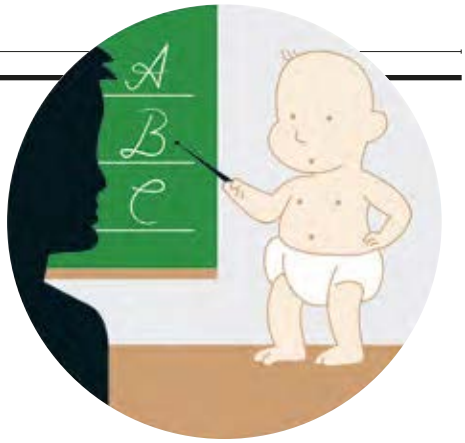
JOHAN ORDONEZ *Getty Images*

Soil moisture is a key factor that can transform a flash flood into a landslide: a heavy storm assaulting already wet soil is riskier than the same storm falling on drier soil, says civil engineer Jacqueline Rivera of El Salvador's Ministry of Environment and Natural Resources, who also is testing the landslide-forecast system.

This is why El Cambray II was so important: it was the first event of its kind to occur after the landslide component was added to the flash-flood forecasts for validation. Once the storm had passed, researchers quickly saw that the enhanced system had identified El Cambray II as being at high risk for a landslide throughout the 2015 storm. The event also gave them an opportunity to closely study the postslide conditions on the ground and compare them with the satellite-based prediction. Landslide "nowcasts" are maturing elsewhere, too. Geomorphologist Dalia B. Kirschbaum of the NASA Goddard Space Flight Center and her colleagues published online a global system that integrates the agency's weather satellite data with a similar landslide-prediction model. NASA plans to use the system to aid humanitarian organizations such as the World Food Program and the International Committee of the Red Cross in disaster-response planning.

Meanwhile all seven Central American countries are calibrating how well the HRC landslide models mesh with local historical and real-time landslide data. Later HRC will use funds from the U.S. Agency for International Development to train civil defense officials in 57 more countries. Currently the models and their forecasts are shared only with disaster-management teams, but Rivera says El Salvador aims to validate it during this summer's rainy season and subsequently put it to regular use for public warnings.

If the better-targeted warnings provided by these systems continue to prove accurate, they may start earning residents' trust and, more important, saving lives. —*Lucas Laursen*



COGNITIVE SCIENCE

Bilingual Brains Remember

Adopted children retain early exposure to a language without knowing it

New evidence suggests that the earliest traces of a language can stay with us into adulthood, even if we no longer speak or understand the language itself. And early exposure also seems to speed the process of relearning it later in life.

In the new study, recently published in *Royal Society Open Science,* Dutch adults were trained to listen for sound contrasts in Korean. Some participants reported no prior exposure to the language; others were born in Korea and adopted by Dutch families before the age of six. All participants said they could not speak Korean, but the adoptees from Korea were better at distinguishing between the contrasts and more accurate in pronouncing Korean sounds.

"Language learning can be retained subconsciously, even if conscious memories of the language do not exist," says Jiyoun Choi, postdoctoral fellow at Hanyang University in Seoul and lead author of the study. And it appears that just a brief period of early exposure benefits learning efforts later; when Choi and her collaborators compared the results of people adopted before they were six months old with results of others adopted after 17 months, there were no differences in their hearing or speaking abilities.

"It's exciting that these effects are seen even among adults who were exposed to Korean only up to six months of age—an age before which babbling emerges," says Janet Werker, a professor of psychology at the University of British Columbia, who was not involved with the research. Remarkably, what we learn before we can even speak stays with us for decades. —*Jane C. Hu*

Illustrations by Thomas Fuchs

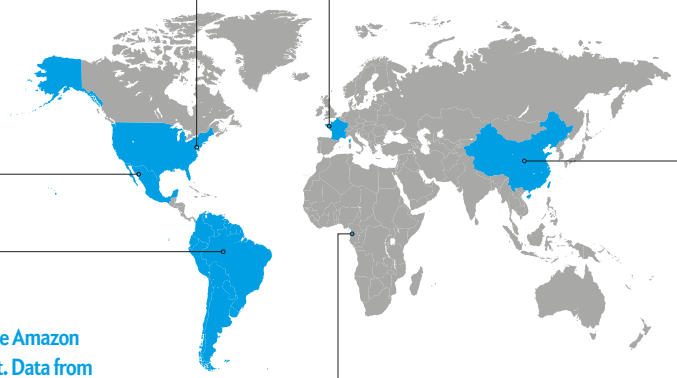
IN THE NEWS

Quick Hits

U.S.
A ballet about space travel will premiere this month at the John F. Kennedy Center for the Performing Arts in Washington, D.C. Classical dance superstar Ethan Stiefel visited NASA headquarters to research the piece.

FRANCE
Pyrethroid insecticides may be affecting children's behavior in the region of Brittany. Six-year-olds whose urine contained the chemical or whose mothers' urine contained it during pregnancy were more likely to behave abnormally.

MEXICO
Only 30 vaquitas—small porpoises that live exclusively in the Gulf of California—remain in the wild, according to a recent report. The marine mammals get trapped in illegal gill nets set to catch totoaba fish, another endangered species.



CHINA
The frequency of hail storms, thunderstorms, high winds and other severe weather events dropped by nearly half on average across the nation from 1961 to 2010, a recent study concludes. Climate change and air pollution could play a role.

SOUTH AMERICA
Indigenous peoples may have shaped the Amazon rain forest more than previously thought. Data from 1,000 forest plots show that trees known to have been cultivated—such as cacao, acai and Brazil nut—are more common in the Amazon basin than nondomesticated trees.

EQUATORIAL GUINEA
A new insight could help efforts to control the spread of malaria, which has developed resistance to the go-to drug artemisinin. Thanks to genome sequencing, researchers now know that the gene mutation that caused the first case of artemisinin-resistant malaria originated in West Africa.

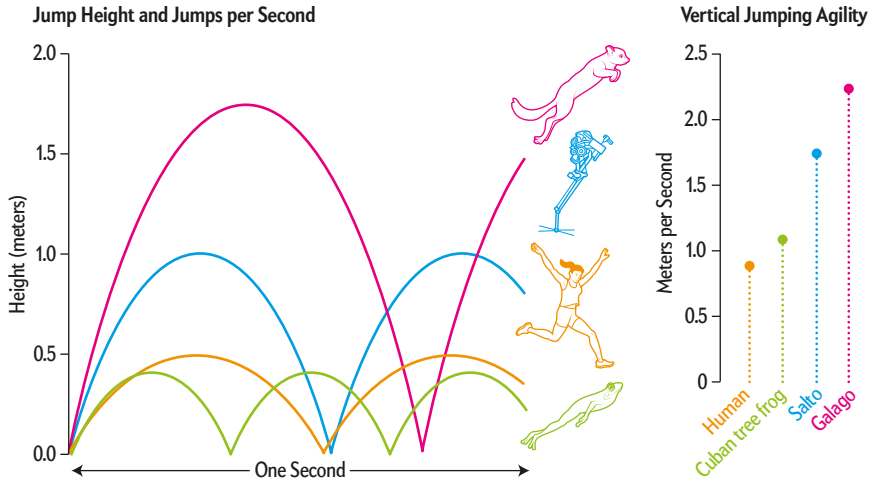
—Andrea Marks

For more details, visit
www.ScientificAmerican.com/may2017/advances

TECHNOLOGY

High Robot

Mimicry of a small African mammal enabled the development of a more agile robot



To develop Salto, researchers studied the jumping behavior of several animals, including the galago, a small African primate with remarkable agility. Jumpers were compared using vertical jumping agility, a metric that combines height and the number of jumps done in one second.

SOURCE: "ROBOTIC VERTICAL JUMPING AGILITY VIA SERIES-ELASTIC POWER MODULATION," BY DUNCAN W. HALDANE ET AL., IN *SCIENCE ROBOTICS*, VOL. 1, NO. 1, ARTICLE NO. EAAG2048; DECEMBER 6, 2016

Robots are notoriously lousy jumpers. Some can jump high, but not repeatedly, over a short period. And vice versa. Duncan Haldane, a roboticist and Ph.D. student at the University of California, Berkeley, realized one implication of this shortcoming—many existing bots cannot maneuver large gaps and high hurdles at, say, a disaster site where they are doing rescue work. So Haldane turned to the animal kingdom to study nature's best jumpers, hoping to select one as a model for a more agile, autonomous machine.

Haldane started by creating a measure to assess both how high and how rapidly an animal could jump. His further research determined that nature's best continuous jumper is the galago, or bush baby, a nocturnal primate native to Africa. The galago's agility metric was twice that of any contemporary jumping robot. The results were detailed in a recent issue of *Science Robotics.*

The galago's legs and muscles are optimized for crouching, a position that helps it store potential energy in its tendons. Haldane translated those physics to fashion a robot he named Salto. It weighs just 100 grams (about the mass of a bar of soap) and has a one-meter vertical jump. But more remarkably it can jump off a floor to a target on a wall and ricochet an average of another 1.21 meters higher. The mechanics of the new jumping system, Haldane says, could be applied to any robot. And that means it is only a matter of time before more of our mechanical friends can leap tall buildings, at least in multiple bounds.

—Erin Biba

ENERGY

Green Hydrogen

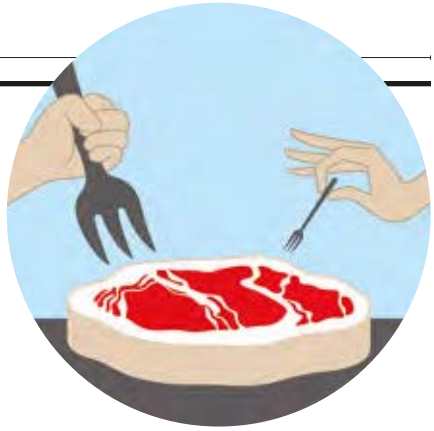
A viable solar-powered approach for making hydrogen fuel might be within reach

Hydrogen is currently used to upgrade crude oil and synthesize ammonia, a critical building block of the fertilizers applied in modern agriculture. It also could be valuable as a feedstock for generating green electricity and as an ingredient in environmentally friendly fuel cells to power cars and trucks. But hydrogen is commonly produced from natural gas heated by steam, which results in greenhouse gas emissions and other environmental problems. Thus, scientists have been working to replace this process with one that taps a renewable energy source—and just such a breakthrough was announced in a paper recently published in *Nature Energy.*

The new approach relies on a photoelectrochemical (PEC) device, a type of solar cell that can potentially split water molecules more efficiently than other methods. Scientists have long struggled to design a PEC device that is both efficient and durable enough to be cost-effective. A key advance came 18 years ago, when John Turner, an electrochemist at the U.S. National Renewable Energy Laboratory, designed a device that comprised layers of gallium indium phosphide and gallium arsenide semiconductors. These materials convert sunlight to electricity more efficiently than other options. Turner's design held the record for the highest solar-to-hydrogen conversion efficiency until 2015. But the acidic solution to which the cell was exposed while in use quickly broke it down, making the hydrogen it produced too expensive.

For the new design, researchers led by chemist Jing Gu of San Diego State University added coatings to the semiconductor layers to prevent acid corrosion. These protective coatings significantly extended the life of Turner's high-efficiency design and produced a PEC device that retains 80 percent of its capabilities in durability tests. A "hydrogen economy" in which consumers can make their own hydrogen to power their cars and heat or cool their homes may not yet be imminent, but at least this engineering feat makes such a future sound a little less like utopian hype. *—Melissa C. Lott*

Graphic by Brown Bird Design (figures) and Amanda Montañez (graphs)



ANTHROPOLOGY

Of Meat and Men

Ancient bones may hold clues to the origins of male domination in society

"Women and lowly men are so hard to handle. If you let them too close to you, they become disobedient. But if you keep them at a distance, they become resentful," Confucius is quoted as saying in the *Analects,* a collection dating back to the fifth century B.C. Confucius did not invent gender bias, of course, nor did he devise its systemic expression in patriarchy. But the answer to when the concentration of social power in men first arose, and why, may lie in the bones of his ancestors.

The clue shows up in connective tissue, or collagen, examined during a recent study involving bones from 175 Neolithic and Bronze Age people who lived in China. A carbon signature in this protein suggests the types of grains the people consumed, and a nitrogen signature reveals the proportion of meat in their diet, according to research published in January in the *Proceedings of the National Academy of Sciences USA*.

The bone chemistry indicates that male and female diets were similar during the Neolithic period, which started about 10,000 years ago and in which agriculture began. Both sexes ate meats and grains. "During early farming, females contributed a lot to food production. [Men and women] eat the same things, and they're of more or less equal standing," says Kate Pechenkina, an archaeologist at Queens College, City University of New York, and senior author on the paper.

The menu shift began at the end of the Neolithic and continued through the Bronze Age, often estimated to have begun in China around 1700 B.C. People there increasingly planted wheat, which leaves a carbon signature distinct from that of the millet they had already been growing. The osteoanalysis shows that between 771 and 221 B.C. men continued eating millet and meat—but the latter disappeared from women's diets and was replaced with wheat. Women's bones also began showing cribra orbitalia, a type of osteoporosis and an indicator of childhood malnutrition. "It means already from early childhood, young girls are treated very poorly," Pechenkina says.

Some anthropologists have a theory for why the balance of power tipped just as wheat was introduced, as well as other commodities such as cattle and bronze. These new resources afforded opportunities for wealth to accumulate and may have provided an opening for men to take control of the novel foods and wares—and to use their new power to suppress women.

Violence may have played a role, too. "The [end of China's Bronze Age] is called the Warring States Period," says Stanley H. Ambrose, an anthropologist at the University of Illinois at Urbana-Champaign, who was not involved with the study. In civilizations rife with bloodshed, a warrior class often inflates the value of men, Ambrose explains.

Early China, in particular, may have been primed for patriarchy. "If you're going to develop an empire that's expansive, whether a state in the Andes or in China, that's usually on the back of an army," says Jane Buikstra, an archaeologist at Arizona State University, who was not involved with the study. She thinks that the ambitions of ancient Chinese dynasties, in cahoots with men seeking to control the new resources of the Bronze Age, may have all set the table for a culture of female subordination.

This theory should not be interpreted deterministically. Cultures might take different paths toward social inequality. And elements of these systems can be dismantled. For example, increasing pay parity may be leading to broadly diminishing gender bias in the Western world.

Nevertheless, the early bias evidence in China extends beyond bones. Women's graves started to include fewer burial treasures than men's during the Bronze Age, suggesting females were also treated poorly in death. "That argues it's a lifetime of [gender] distinction," Buikstra says.

—Angus Chen

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Aspirin vs. Cancer

In addition to relieving headaches and preventing heart attacks, the drug seems to keep malignant cells from spreading

By Viviane Callier

If ever there was a wonder drug, aspirin might be it. Originally derived from the leaves of the willow tree, this mainstay of the family medicine cabinet has been used successfully for generations to treat conditions ranging from arthritis to fever, as well as to prevent strokes, heart attacks and even some types of cancer, among other ills. Indeed, the drug is so popular that annual consumption worldwide totals about 120 billion tablets.

In recent years scientists have discovered another possible use for aspirin: stopping the spread of cancer cells in the body after an initial tumor has already formed. The research is still developing, but the findings hint that the drug could one day form the basis for a powerful addition to current cancer therapies.

Not everyone responds equally well to the drug, however, and for some people it can be downright dangerous. Investigators are thus trying to develop genetic tests to determine who is most likely to benefit from long-term use of aspirin. The latest research into the drug's cancer-inhibiting activity is generating findings that could possibly guide those efforts.

MYRIAD MECHANISMS

DURING THE PAST CENTURY researchers demonstrated that aspirin inhibits the production of certain hormonelike substances called prostaglandins. Depending on where in the body these prostaglandins are produced, they may trigger pain, inflammation, fever or blood clotting.

Obviously no one wants to block these natural responses all the time—particularly as they help the body to heal from cuts, bruises, infections and other injuries. But sometimes they linger for too long, causing more harm than good. Long-lasting, or chronic, inflammation, for example, increases the risk of developing heart disease and cancer by causing repeated damage to otherwise normal tissue. Eventually the damaged tissue, depending on where it is located and a host of other factors, may become a vessel-clogging plaque in a coronary artery or a tiny tumor hidden deep within the body. By turning down the prostaglandin spigot, aspirin prevents thousands of heart attacks every year and probably stops a significant number of tumors from forming in the first place.

In 2000 scientists discovered a second major mechanism of action for aspirin in the body. The drug boosts the production of molecules called resolvins, which also helps to quench the fires of inflammation.

More recently, investigators have started to elucidate a third way that aspirin works—one that interferes with the ability of cancer cells to spread, or metastasize, through the body. Intriguingly, in this case, the drug's anti-inflammatory properties do not appear to play the starring role.

Metastasis is a complex process that, somewhat counterintuitively, requires a certain amount of cooperation between tumor cells and their host. Some number of malignant cells must break away from the original tumor, cross the walls of a nearby blood vessel to enter the bloodstream and avoid getting detected by immune system defenders as they travel about the body. Those that survive this gauntlet must then cross the walls of another blood vessel at a different location in the body, nestle into surrounding tissue that is completely different from their original birthplace and start to grow.

Elisabeth Battinelli, a hematologist at Brigham and Women's Hospital in Boston, has shown that cells called platelets, which are better known for their ability to trigger blood clots, also have an important part in allowing tumor cells to spread. First malignant cells coopt certain chemical signals from the platelets that collect along the blood vessel wall. Instead of directing the repair of a potential breach in the wall, however, these repurposed signals help the cancer cells break through the barrier and sneak into the

Illustration by Sara Gironi Carnevale

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bloodstream. Then the cancer cells cloak themselves in a protective layer of platelets to hide from the patrolling sentries of the immune system. Once the tumor cells leave the bloodstream at some distant location, they instruct the platelets that have come along with them to produce so-called growth factors that trigger the development of new blood vessels, essential avenues that carry nutrients and oxygen to the now thriving secondary tumor.

Researchers often inject tumor cells into the bloodstream of mice to approximate what happens during metastasis when cancer cells must navigate the bloodstream to find a new home in the body. When Battinelli and her team fed aspirin to certain strains of mice and then injected them with malignant cells, the investigators discovered that the platelets did not shield breakaway cancer cells from the immune system or produce the necessary growth factors that allow cancer cells to grow and divide in a new location. Thus, aspirin appears to fight cancer in two ways: its anti-inflammatory action prevents some tumors from forming, and its antiplatelet properties interfere with some cancer cells' ability to spread.

Investigators have identified about 60 genes that are turned on or off in response to aspirin.

REWIRING PLATELETS

HOW DOES ASPIRIN STOP tumor cells from hijacking platelets to do their bidding? Instead of blocking a single compound (a prostaglandin, for example), in this case the drug seems to turn entire groups of genes on or off in the nuclei of certain blood cells.

To try to better understand this previously unknown effect of aspirin, cardiologist Deepak Voora of Duke University and his colleagues looked at cells called megakaryocytes, which give rise to platelets. Using complex mathematical and pharmacological tools, they identified about 60 genes that are either turned on or off in the megakaryocytes in response to aspirin. The end result of all this genetic manipulation: the platelets produced by the megakaryocytes did not clump together, which presumably prevented them from camouflaging cancer cells. Thus, in addition to blocking prostaglandins, aspirin basically "rewires the platelets" so that they do not serve as inadvertent accomplices to metastasis.

There is still a lot of basic research that must be conducted, Voora says, before the feasibility of an aspirin-based therapy to prevent metastasis can be determined. The next steps are to confirm these experiments in larger, more diverse groups of people and to better understand the normal functions of these aspirin-sensitive genes. In the meantime, investigators hope to learn enough to create a genetic test that will make it possible to tell whether a patient might benefit from taking aspirin. Ideally, such a test would determine not only the most effective dose of the drug but also whether or not the person's body is reacting to the medication as predicted.

Much of aspirin's cardiovascular benefit, for example, stems from its ability—at a dose as low as 81 milligrams—to prevent clots from forming in the bloodstream. And yet one study of 325 people found that aspirin has no effect on the clotting processes of 5 percent of patients who consume the drug, with another 24 percent having a reduced effect. Furthermore, some people may experience severe side effects—such as bleeding. Thus, no responsible clinician would advise everyone to take the drug on a daily basis.

To date, the only way to know for sure that a patient is resistant to aspirin's anticlotting effects is to test the person's blood after several weeks of therapy to see if it takes longer to form clots than it once did—an expensive proposition that is not very practical. Genetic tests would presumably be less expensive, but they are a long way off. "It's challenging to develop a single molecular test that will tell you if someone will respond [to aspirin] or not because it's become clear that there is no single pathway by which aspirin works," says Andrew Chan, an epidemiologist at Harvard Medical School. In other words, researchers and physicians will have to look at many different genes—and their complex interactions—to determine how likely a patient is to benefit from aspirin treatment, whether for cardiovascular disease or cancer.

Until then, the U.S. Preventive Services Task Force, a national panel of independent health experts, recommends low-dose aspirin to prevent cardiovascular disease and colorectal cancer in only a very select group of people. Those who may benefit the most, according to the available evidence, are adults aged 50 to 59 years who are likely to live at least another decade, have a 10 percent or greater risk of having a heart attack or stroke in that time, are not at increased risk for bleeding (because of other medications, for example) and are willing to take low-dose aspirin daily for at least 10 years. For adults aged 60 to 69 years, the task force recommends selectively offering aspirin treatment depending on individual circumstances. It has determined that there is not enough evidence to weigh the potential benefits against possible harms for daily aspirin use in adults younger than 50 years or older than 70.

Most patients who have already suffered a heart attack or stroke, however, seem to benefit from regular aspirin therapy regardless of age, says Paul Gurbel, director of the Inova Center for Thrombosis Research and Translational Medicine in Falls Church, Va. And if you think you are currently suffering a heart attack, many doctors recommend chewing a 325-milligram tablet of aspirin immediately after you have called 911 to minimize the damage from any potential clot.

Nevertheless, aspirin cannot make up for a lifetime of bad habits. Quitting smoking—or better yet, never starting—eating moderately, keeping your body lean and remaining physically active may be as effective as—or even more effective than—taking aspirin on a daily basis for keeping lots of health problems, including heart disease and cancer, at bay. Aspirin may well be an amazing drug, but it is still not a cure for everything that ails you. SA

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

Building a Better Battery

They've been getting better for decades—but we've been demanding more of them

By David Pogue

"Every technology has improved over the years except batteries! Why can't someone invent a better battery?" Man, if I had a nickel for every time I've heard someone say that—well, I'd have about $17.50.

In fact, though, the average gadget fan is missing three huge points about batteries. (In February, PBS aired a *NOVA* special called "Search for the Super Battery," of which I was the host. After a year of visiting laboratories and interviewing scientists, I can admit that batteries are on my mind these days.)

First point: The batteries you probably think about most are the ones in your phone or laptop. But you could argue—and many scientists do—that batteries are the keys to tackling much, much bigger problems, like energy, transportation and climate change.

For example, today electric cars represent only about 1 percent of U.S. new car sales. One reason is they cost more than gas-powered cars. Another is range anxiety—consumers' fear they'll run out of charge far from home. The cheaper, higher-capacity batteries now under development aim to solve both those problems.

Then there's the grid. Electricity isn't like water, waiting in the pipe until you turn on the faucet. When you turn on a lamp, that power must be generated *right now,* in real time. As a result, electric utilities spend their days coping with gargantuan swings in energy demand. There's almost no demand at night, when everyone's asleep, and then tremendous spikes at 5 P.M., when people get home from work. Utilities actually maintain expensive, inefficient, sporadically used backup power plants ("peaker plants") just to handle demand surges, as occur during heat waves.

Batteries connected to the grid could even out those absurd swings. Maybe even more important, grid batteries could capture solar power while the sun's shining—and wind power when it's blowing—for use when we really need it. Thus far we haven't been able to make the sun and wind respect our lifestyle schedules.

The second point people miss: Our complaints tend to be about our batteries' capacity: how long our gadgets run between charges. But in fact, capacity (energy density) is only one item on the industry's wish list. We also want batteries to be cheap, environmentally benign after they're used up, long-lived (that is, able to be recharged thousands of times), compact, light (especially for electric cars) and safe. An exploding phone can ruin your whole day, as Samsung could attest.

In general, you can't have it all in a single battery. Then again, you don't always need it all. Grid batteries, for example, don't have to be portable or compact. So the door is open for the dawn of, say, flow batteries, in which chemicals, stored in huge tanks, flow past one another inside a reaction chamber. Or flywheel batteries, in which disks made of material such as steel and weighing thousands of pounds spin thousands of times per minute in a friction-free chamber (suspended by a magnet in a vacuum) at night, when the energy to keep them spinning is cheaper, so that engineers can reclaim the kinetic energy as power during the day.

The third important point: Batteries *have* been getting better over the decades. The reason we don't notice is that our devices have been getting faster, more powerful and more power-hungry at the same time. Heck, if you could put a modern iPhone battery into a 1995 phone, it'd probably go a year on a single charge.

Other great things are on the way. Materials scientist Mike Zimmerman has succeeded in replacing the highly flammable liquid electrolyte (through which ions swim when you charge or discharge your battery) with a single piece of special plastic film. Presto: a battery incapable of igniting or exploding. And because it's unblowuppable, Zimmerman can use lithium metal instead of lithium-ion chemistry, which has a much higher energy density but is considered too dangerous to use with today's liquid-electrolyte batteries. Presto: longer life.

So if you do want to complain about your batteries, get it out now. It won't be long before they have a much better reputation. SA

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Illustration by Jay Bendt

ARCHAEOLOGY

THE NEW ORIGINS OF TECHN

ARCHAEOLOGISTS at a site in northwestern Kenya called Lomekwi 3 have unearthed the oldest stone tools in the world.

Photographs by Andrew Renneisen

OLOGY

ANCIENT STONE TOOLS FROM KENYA SHATTER THE CLASSIC STORY OF WHEN AND HOW HUMANS BECAME INNOVATORS

By Kate Wong

The desert badlands on the northwestern shores of Kenya's Lake Turkana offer little to the people who live there. Drinking water is elusive, and most of the wild animals have declined to near oblivion. The Turkana scrape by as pastoralists, herding goats, sheep, cattle, donkeys and the occasional camel in the hot, arid countryside. It is a hard life. But millions of years ago the area brimmed with freshwater, plants and animals. It must have been paradise for the human ancestors who settled here.

Kate Wong is a senior editor at *Scientific American.*

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Sonia Harmand has come to this region to study the legacy these ancestors left in stone. Harmand is an archaeologist at Stony Brook University. She has an intense gaze and a commanding presence. On a hazy July morning Harmand sits at a small, wood folding table, scrutinizing a piece of rock. It is brownish-gray, about the size of her pinkie fingernail, and utterly unremarkable to the untrained eye. But it is exactly what she has been looking for.

Nearby 15 workers from Kenya, France, the U.S. and England are digging their way into the side of a low hill. They tap hammers against chisels to chip away at the buff-colored sediments, searching for any bits of rock that could signal ancient human activity. At the top of the hill, the workers' water bottles hang like Christmas ornaments on the thorny branches of an acacia tree; the early breeze will keep their contents cool a little longer before the heat of the day sets in. By afternoon the air temperature will top 100 degrees Fahrenheit, and the excavation floor, windless and sun-cooked, will live up to its nickname: the Oven.

In 2015 Harmand and her husband, Jason Lewis, a paleoanthropologist at Stony Brook, announced that their team had discovered 3.3-million-year-old stone tools at this site, which is called Lomekwi 3. They were the oldest stone tools ever found by far—so old that they challenged a cherished theory of human evolution. The scientists want to learn who made the tools and why. But they also have a more immediate task: unearthing more evidence that the tools are, in fact, as old as they appear.

The fragment in Harmand's hand is the first evidence of ancient stone-tool production the researchers have recovered since they got here. It is a piece of debris produced by knapping—the act of striking one rock against another to produce a sharp-edged flake. Small and light, the fragment implies that the site has not been disturbed by flowing water in the millions of years since. That fact, in turn, supports the argument that the Lomekwi 3 tools come from this ancient sedimentary layer and not a younger one. Now that the excavators have hit the artifact-bearing level of the site, they must proceed with care. "*Pole pole,*" Harmand instructs them in Swahili. Slowly, slowly.

Paleoanthropologists have long viewed stone-tool production as one of the defining characteristics of the *Homo* genus and the key to our evolutionary success. Other creatures use tools, but only humans shape hard materials such as rock to suit their purposes. Moreover, humans alone build on prior innovations, ratcheting up their utility—and complexity—over time. "We seem to be the only lineage that has gone fully technological," says Michael Haslam of the University of Oxford. "It isn't even a crutch. It's like an addition to our bodies."

The conventional wisdom holds that our techno dependence began to form during a period of global climate change between three million and two million years ago, when Africa's woodlands transformed into savanna grasslands. Hominins, members of the human family, found themselves at a crossroads. Their old food sources were vanishing. They had to adapt or face extinction. One lineage, that of the so-called robust australopithecines, coped by evolving huge molars and powerful jaws to process the tougher plant foods available in grassland environments. Another—the larger-brained *Homo*—invented stone

IN BRIEF

A traditional view of human evolution holds that stone-tool technology originated with members of our genus, *Homo,* as an adaptation to shifting climate.

In this scenario, that adaptation quickly helped to establish a feedback loop that dramatically expanded brain size and technological prowess in our lineage.

Recently discovered stone tools from Kenya that date to 3.3 million years ago—long before the oldest known *Homo* fossils—have overturned this scenario.

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WORKERS DIG into the side of a hill at Lomekwi 3 in July 2016, looking for artifacts (*1*). They sift each bucket of sediment they remove, hoping to recover even the smallest fragments of interest (*2*). Every pebble is studied for signs of human modification.

tools that gave it access to a wide variety of food sources, including the animals that grazed on these new plants. With the rich stores of calories from meat, *Homo* could afford to fuel an even bigger brain, which could then invent new and better tools for getting still more calories. In short order, a feedback loop formed, one that propelled our brain size and powers of innovation to ever greater heights. By one million years ago the robust australopithecines disappeared, and *Homo* was well on its way to conquering the planet.

The Lomekwi tools have smashed that scenario to pieces. Not only are they too old to belong to *Homo,* but they also predate the climate shift that supposedly kindled our ancestors' drive to create. And without any cut-marked bones or other signs of butchery at the site, it is not at all certain that the tools were used to process animal foods. What is more, such a vast expanse of time separates the Lomekwi tools from the next oldest implements on record that it is impossible to connect them to the rest of humanity's technological endeavoring, suggesting that the advent of stone tools was not necessarily the watershed moment that experts have always envisioned it to be.

These new discoveries have scientists scrambling to figure out when and how our predecessors acquired the cognitive and physical traits needed to conceptualize and fashion stone tools and to pass their craft to the next generation. If multiple lineages made tools from rock, researchers will need to rethink much of what they thought they knew about the origins of technology and how it shaped our branch of the family tree.

DAWN BREAKS GENTLY IN THE BUSH—A SLOW brightening of sky, a creeping swell of birdsong—and the team's campsite, on the bank of a dry riverbed about a mile from Lomekwi 3, comes to life. By 6:30 A.M. the workers emerge from their tents and head to the makeshift dining table for breakfast, walking along a gravel path lined with stones to deter the snakes and scorpions. Within the hour they pile into Land Cruisers and set off on a bone-rattling ride to the excavation.

The team is down one vehicle and short on seats in the remaining two, so archaeologist Hélène Roche has decided to stay at camp. Roche is an emeritus director of research at the French National Center for Scientific Research and an expert in early stone-tool technologies. She has short, sand-colored hair, and she dresses in desert hues. Her voice is low and crisp. Roche led the archae-

Map by Amanda Montañez

ological research in western Turkana for 17 years before handing the reins to Harmand and Lewis in 2011. She has returned for the second half of this expedition to see how they are faring. I remain at camp for the day to ask her about the history of work in this region.

"When I started in archaeology, we were just getting used to having stone tools at 1.8 [million years ago] at Olduvai," Roche recalls. In 1964 Kenyan paleoanthropologist Louis Leakey announced that he had found *Homo*-like fossils in association with what were then the oldest known artifacts in the world, stone tools from Tanzania's Olduvai Gorge (referred to as Oldowan tools). He assigned the fossils to a new species, *Homo habilis,* the "handy man," cementing the idea that stone toolmaking was linked to the emergence of *Homo*.


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Hints that stone tools might have originated before *Homo* soon arrived, however. In the 1970s Roche, then a graduate student, discovered older Oldowan stone tools at a site in Ethiopia called Gona. When archaeologist Sileshi Semaw, now at the National Center for Research on Human Evolution in Burgos, Spain, and his colleagues eventually analyzed the tools, they reported them to be 2.6 million years old. Because no hominin remains turned up with the tools, researchers could not be sure which species made them. Semaw and his team proposed that a small-brained australopithecine species found at a different site nearby—*Australopithecus garhi*—was the toolmaker. Few were swayed by that argument, however. *Homo* was still the favorite candidate, even though, at the time, the oldest known *Homo* fossil was only 2.4 million years old. (A recent find has extended the fossil record of *Homo* back to 2.8 million years ago.)

Yet as old as they were, the Gona artifacts looked too skillfully wrought to represent humanity's first foray into stone-tool manufacturing. So did other ancient tools that began to emerge, including some from western Turkana. In the 1990s Roche found 2.3-million-year-old Oldowan stone tools at a site five miles from here known as Lokalalei 2c. She realized that in many instances, the site preserved entire knapping sequences that she could piece together like a 3-D puzzle. By refitting the Lokalalei flakes to the cores from which they were detached, Roche and her colleagues could show that toolmakers struck as many as 70 flakes from a single core. This impressive feat required an understanding of the rock shape best suited to flaking (flat on one side and convex on the other) and careful planning to maintain that shape while knapping. "You cannot imagine what it is like to hold the pieces together and reconstruct what [the toolmaker] has done and how he has done it, to go inside the prehistoric mind," she says.

It was becoming clear that the sophistication evident in the tools from Gona, Lokalalei and elsewhere could not have sprung fully formed from the minds of these knappers. Some kind of technological tradition must have preceded the Oldowan.

In 2010 far older signs of stone-tool technology came to light. Zeresenay Alemseged, now at the University of Chicago, and his colleagues reported that they had found two animal bones bearing what appeared to be cut marks from stone tools at the site of Dikika in Ethiopia. The bones dated to 3.4 million years ago, hundreds of thousands of years before the earliest known traces of *Homo*. The researchers credited the marks to *Australopithecus afarensis,* a species that was still apelike in many respects, with about as much gray matter as a chimpanzee has and a body that retained some adaptations to life in the trees—hardly the brainy, fully terrestrial hominin that researchers had traditionally expected the first butcher to be. The claims did not go unchallenged, however. Some experts countered that animals could have trampled the bones. Without the stone tools themselves, the critics argued, the Dikika scars could not qualify as tool-inflicted marks—and the question of just how far back in time technology originated remained unresolved.

Around the time the battle over the Dikika bones erupted, Harmand and Lewis began to hatch a plan to look for the older stone tools that the Dikika marks, along with the too-good-to-be-first tools from Gona and Lokalalei, implied should exist. In the summer of 2011 they set out in search of new archaeological sites on the western side of Lake Turkana.

The Turkana basin, as well as much of the Great Rift Valley in which it sits, is a paleoanthropologist's dream. Not only does it harbor an abundance of fossils and artifacts, but it preserves them in rocks that, with some sleuthing, can be dated with a relatively high degree of certainty. The region's history of volcanic eruptions and fluctuating water levels is recorded in the layers of sediment that have accumulated over eons to form a sort of layer cake. Water and wind erosion have exposed cross sections of the cake in locations throughout the basin. Tectonic activity has pushed some sections higher and other sections lower than they once were, but as long as any given exposure preserves at least a few layers of the cake, researchers can figure out where in the geologic sequence it comes from and thus how old it is.

EXCAVATORS CHIPPED away at the sediments for weeks before finding any artifacts (*1*). The first finds were flakes produced incidentally during knapping (*2*). A volcanic ash layer called the Toroto Tuff helped to establish the age of the site (*3*).

To navigate the rough, roadless landscape, the team drives in the dry riverbeds, called *lagas,* that snake through the region, running from the lake to points west. On July 9 of that year the researchers were headed to a site where, 12 years earlier, a different team had found a 3.5-million-year-old skull of another hominin species, *Kenyanthropus platyops,* when they took the wrong branch of the Lomekwi *laga* and got lost. Climbing a nearby hillside to get a better view of the terrain, they realized that they had ended up in just the kind of place that is promising for finding ancient remains. Outcrops of soft lake sediments, which tend to preserve fossils and artifacts well, surrounded them. And the researchers knew from previous geologic mapping of the region that all the sediments along this *laga* were more than 2.7 million years old. They decided to look around.

Within a couple of hours Sammy Lokorodi, one of the Turkana members of the team, found several rocks bearing hallmarks of knapping—adjacent, scoop-shaped scars where sharp flakes had been chipped off. Could these be the older, more primitive tools that the team was looking for? Maybe. But the tools were found on the surface. A modern-day human—perhaps a passing Turkana nomad—could have made them and left them there. The researchers knew that to make a convincing case that the tools were ancient, they would have to find more of them, sealed in sediments that had lain undisturbed since their deposition, and conduct detailed geologic analyses of the site to establish the age of the artifacts more precisely. Their work had just begun.

By the time the researchers went public with their discovery, describing it in 2015 in *Nature,* they had excavated 19 stone tools from a 140-square-foot area. And they had correlated the position of the sediment layer that held the tools to layers of rock with known ages, including a 3.31-million-year-old layer of compacted volcanic ash called the Toroto Tuff and a magnetically reversed layer from a time, 3.33 million years ago, when the earth's magnetic poles switched places. They had also located the source of the raw material for the tools—a 3.33-million-year-old layer of beach containing cobbles of volcanic basalt and phonolite, along with fish and crocodile fossils that show just how much higher lake levels were back then as compared with today. Together these clues indicated that the tools dated to a stunning 3.3 million years ago—700,000 years older than the Gona tools and half a million years older than the earliest fossil of *Homo*.

The artifacts have little in common with Oldowan tools. They are far larger, with some flakes the size of a human hand. And experiments indicate that they were knapped using different techniques. Oldowan knappers favored a freehand style, striking a hammerstone held in one hand against a core held in the other, Harmand explains. The Lomekwi knappers, in contrast, would either bang a core they held in both hands against an anvil lying on the ground or place a core on the anvil and hit it with a hammerstone. The methods and finished products demonstrate an understanding of the fracture mechanics of stone but show considerably less dexterity and planning than are evident in tools from Gona and Lokalalei. The researchers had found their pre-Oldowan stone-tool tradition. They call it the Lomekwian.

NOT EVERYONE IS CONVINCED THAT THE LOMEKWI tools are as old as the discovery team claims. Some skeptics contend that the team has not proved that the artifacts originated from the sediments dated to 3.3 million years ago. Discoveries made this field season, including the knapping debris, as well as a handful of new tools recovered during excavation, may help allay those concerns. But even researchers who accept the age and the argument that the rocks were shaped by hominins are grappling with what the find means.

First, who made the tools? To date, the team has not recovered any hominin remains from the site, apart from a single, enigmatic tooth. The age and geographical location of the tools

suggest three possibilities: *K. platyops,* the only hominin species known to have inhabited western Turkana at the time; *A. afarensis,* the species found in association with the cut-marked animal bones from Dikika; and *Australopithecus deyiremeda,* a species that was recently named, based on a partial jawbone found in Ethiopia. Either *K. platyops* or *A. afarensis* would be surprising because both those species had a brain about the size of a chimp's—not the enlarged brain researchers thought the first toolmaker would have. (*A. deyiremeda*'s brain size is unknown.)

Small brain size is not the only anatomical trait that experts did not expect to see in an ancient knapper. Paleoanthropologists thought that tool use arose after our ancestors had abandoned life in the trees to become committed terrestrial bipeds. In this scenario, only after their hands had been freed from the demands of climbing could hominins evolve the hand shape needed to make stone tools. Yet studies of *A. afarensis,* the only one of these three species for which bones below the head have been found, indicate that although it was a capable biped on the ground, it retained some traits that would have allowed it to climb trees for food or safety. Just how important was the shift away from life in the trees to life on the ground in the emergence of stone-tool technology?

The Lomekwi 3 tools are also forcing scientists to reconsider why hominins invented stone tools to begin with. Reconstruction of the paleoenvironment of the greater Lomekwi area 3.3 million years ago indicates that it was wooded, not the savanna experts thought had forged *Homo*'s stone-working skills.

Perhaps the biggest question: Why are the Lomekwi 3 tools so isolated in time? If stone-tool manufacture was the game-changing development that experts have always thought it to be, why did it not catch on as soon as it first appeared and initiate the feedback loop that expanded the brain?

RECENT STUDIES MAY HELP EXPLAIN HOW A HOMININ MORE primitive than *Homo* could have come to make stone tools. It turns out that some of the differences in cognitive ability between hominins and other primates may not be as great as previously thought.

Observations of our closest primate cousins, for example, hint that even though they do not manufacture stone tools in the wild, they possess many of the cognitive abilities needed to do so. David Braun of George Washington University and Susana Carvalho of Oxford have found that in Bossou, Guinea, wild chimps that use stones to crack open nuts understand the physical properties of different rocks. The researchers shipped assorted stones from Kenya to Bossou and made them available to the chimps for their nut-cracking activities. Despite not having prior experience with these kinds of rock, the chimps consistently selected the ones with the best qualities for the job. And experiments with captive bonobos carried out by Nicholas Toth of the Stone Age Institute in Bloomington, Ind., and his colleagues have shown that they can be trained to make sharp flakes and use them to cut rope. "I have no doubt that our apes could replicate what [Harmand and her team] have at Lomekwi, given the right raw material," Toth asserts.

Even inventing stone tools in the first place may not have required special genius. Last fall Tomos Proffitt of Oxford and his colleagues reported that they had observed wild capuchin monkeys in Brazil's Serra da Capivara National Park unintentionally making sharp stone flakes that look for all the world like Oldowan tools. Quartzite cobbles abound in the monkeys' environment, and they will often pick up one cobble and bash it against another embedded in the ground that serves as an anvil. All the bashing dislodges sharp flakes that have the hallmarks of intentionally produced stone tools, including the scooplike shape that arises from what is known as conchoidal fracturing. The monkeys ignore the flakes, however. Instead they seem to be pulverizing the quartz to eat it—they pause between strikes to lick the resulting dust from the anvil. Perhaps early hominins invented their stone flakes by accident, too, or found naturally sharp stones in their environment, and only later, once they found a good use for them, began fashioning them on purpose.

The possibility that the Lomekwi toolmakers had hands that were at once capable of knapping and climbing in trees does not seem so improbable either, once one considers what our primate cousins can manage. The modern human hand, with its short, straight fingers and long, opposable thumb, is purpose-built for power, precision and dexterity—traits we exploit every time we swing a hammer, turn a key or send a text. Yet as the observations of chimps, bonobos and capuchins show, other primates with hands built for grasping tree branches can be surprisingly dexterous. The hands of partially arboreal hominins could have been similarly clever.

In fact, recent studies of the fossilized hand bones of three small-brained hominin species from South Africa—*Australopithecus africanus, Australopithecus sediba* and *Homo naledi*—show evidence for exactly this combination of activities. All three species have curved fingers—a trait associated with climbing. Yet in other respects, their hands look like those of toolmakers. Tracy Kivell and Matt Skinner, both at the University of Kent in England, examined the internal structure of the hand bones, which reflects the loading forces sustained in life, and found a pattern consistent with that seen in hominins known to have made and used stone tools and different from the internal structure of the hand bones of chimps. "Being a good climber and a dexterous toolmaker are not mutually exclusive," Kivell says. A variety of hand shapes can make and use stone tools, she explains. The changes the human hand eventually underwent just optimized it for the job.

FRIDAY IS *CHOMA* NIGHT FOR THE LOMEKWI TEAM—ROASTED goat will be served for dinner. Nick Taylor of Stony Brook, a droll Brit, is taking advantage of the menu to try to figure out what purpose the Lomekwi stone tools served. This morning one of the local Turkana shepherds brought the purchased animal for slaughter. This afternoon, as the sun begins its descent and meal preparations begin, Taylor asks camp kitchen manager Alfred "Kole" Koki to try to process the carcass with replicas of the Lomekwi tools. Koki, an experienced butcher, doubts they will work. But he gamely takes a two-inch-long flake and starts slicing. He manages to skin most of the animal and carves some of the meat with the sharp-edged rocks, discarding them as they become dull, before reclaiming his steel knife to finish the job.

Taylor observes how Koki instinctively holds each flake and how long it retains its edge before Koki requests a new one. Taylor keeps the used replica flakes so that later he and his colleagues can compare their damaged edges with those of the real

SONIA HARMAND and husband, Jason Lewis, co-direct the West Turkana Archaeological Project that discovered Lomekwi 3.

flakes. He will also collect some of the bones to study what kind of cut marks the carving might have left on them. And he will try using the tools to cut plant materials, including wood and tubers. In addition, Taylor is looking for any residues on the Lomekwi tools that might provide clues to what they were processing.

For whatever reason the Lomekwi hominins made stone tools, their tradition does not appear to have stuck. Nearly 700,000 years separates their implements from the next oldest tools at Gona. Perhaps hominins did indeed have a stone-tool culture spanning that time, and archaeologists have just not found it yet. But maybe the Lomekwi stone-working was just a flash in the pan, unrelated to the Oldowan technology that followed. Even the Oldowan record is patchy and variable, showing different tool styles at different times and places, without much continuity among them. As Roche puts it, "There is not one Oldowan but Oldowans."

This pattern suggests to many archaeologists that populations in multiple lineages of hominins and possibly other primates may have experimented with stone-tool production independently, only to have their inventions fizzle out, unbequeathed to the next generation. "We used to think that once you have toolmaking, we're off to the races," observes Dietrich Stout of Emory University. But maybe with these early populations, he says, technology was not important to their adaptation, so it simply faded away.

Around two million years ago, however, something changed. The tools from this period start to look as though they were manufactured according to the same rules. By around 1.7 million years ago a more sophisticated technology arises: the Acheulean. Known for its hand ax, the Swiss Army knife of the Paleolithic, the Acheulean tradition spread across Africa and into other parts of the Old World.

Braun thinks the shift has to do with improved information transmission. Chimps appear to have what he calls low-fidelity transmission of behavior based on observational learning. It works pretty well for simple tasks: by the end of his team's six-week-long experiment with the Bossou chimps, the entire community was using the rocks the same way. The activity seemed to spread by means of a recycling behavior in which one individual, typically a juvenile, would watch another, usually an adult, use a certain type of rock to crack nuts, after which the youngster would try to use the adult's tool set to achieve the same ends.

Modern humans, in contrast, actively teach others how to do complex things—from baking a cake to flying a plane—which is a high-fidelity form of transmission. Perhaps, Braun suggests, the variability seen in the Lomekwi tools and in those of the early Oldowan is the result of lower-fidelity transmission, and the standardization of the later Oldowan and the more sophisticated Acheulean signals the development of a more effective means of sharing knowledge, one that allowed humans to ratchet up their technological complexity.

As ancient as the tools from Lomekwi 3 are, the team suspects that even older ones are out there, awaiting discovery. One day, while the rest of the team is excavating, Lewis, Lokorodi and Xavier Boës, a geologist at the French National Institute for Preventive Archaeological Research, set out to look for them. They head for an area known to have sediments older than those at Lomekwi 3, speeding up the *laga* in a cloud of dust. They are taking the same branch they meant to take on that day five years ago when they lost their way and discovered Lomekwi 3.

When they reach their destination, they fan out, eyes trained on the ground, scanning for signs of human handiwork in a sea of rocks baked red by the sun. Before long, Lokorodi spies cobbles bearing scoop-shaped scars. In theory, they could be more than 3.5 million years old. But the team will have to follow the same painstaking procedures it carried out at Lomekwi 3. The researchers will have to determine whether the rocks have been shaped by humans and, if so, figure out which stratigraphic level they eroded from, pinpoint the age of that level and then find more of them undisturbed in the ground. Lewis photographs the rocks and notes their location for possible survey in the future. The team will also explore a promising area about three miles from Lomekwi 3 that has sediments dating to more than four million years ago.

Figuring out what technology came before and after Lomekwi 3 and getting a clearer picture of how the environment was shifting will be critical to elucidating the correlations among dietary change, tools and the origins of *Homo*. "Maybe the links are all the same, but everything happened earlier," Lewis offers. "The pieces have exploded, but that doesn't mean they won't reassemble."

"We know quite a lot now but not enough," Roche says of the discoveries in western Turkana. "This is only the beginning." SA

MORE TO EXPLORE

3.3-Million-Year-Old Stone Tools from Lomekwi 3, West Turkana, Kenya. Sonia Harmand et al. in *Nature*, Vol. 521, pages 310–315; May 21, 2015.

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scientificamerican.com/magazine/sa

An

ASTROPHYSICS

Alien technology is probably not causing Boyajian's star to dim mysteriously. But alternative explanations are hard to come by

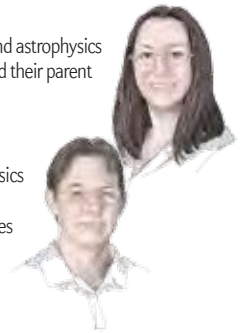
By Kimberly Cartier and Jason T. Wright

Illustrations by Victor Mosquera

STRANGE NEWS FROM other Star

Kimberly Cartier is a senior doctoral student in astronomy and astrophysics at Pennsylvania State University. Her specialty is exoplanets and their parent stars. Cartier also focuses on science communication.

Jason T. Wright is an associate professor of astronomy and astrophysics at the Center for Exoplanets and Habitable Worlds at Penn State and participates in the search for extraterrestrial intelligence. Wright studies exoplanets and the stars they orbit.



ONE QUIET AFTERNOON IN THE FALL OF 2014, JUST AS THE TREES WERE CHANGING FROM GREEN TO gold, Tabetha Boyajian visited our astronomy department at Pennsylvania State University to share an unusual discovery. That landscape on the brink of transformation turned out to be a fitting backdrop for a meeting that would change the course of our careers.

Then a postdoctoral scholar at Yale University, Boyajian had flagged inexplicable fluctuations of light from a star monitored by NASA's planet-hunting Kepler space telescope. The fluctuations looked nothing like those caused by a planet passing between the star and the telescope. She had already ruled out other culprits, including glitches in Kepler's hardware, and she was looking for new ideas. One of us (Wright) suggested something *very* unorthodox: perhaps the fluctuations in brightness were caused by alien technology.

In the 1960s physicist Freeman Dyson postulated that advanced, energy-hungry civilizations might enshroud their home stars in solar collectors—later called Dyson spheres—to absorb practically all of a star's light. Could this fading star be the first evidence that other cosmic cultures were more than science fiction? That outré idea was a hypothesis of last resort, but for the time being, we could not dismiss it.

The star that stumped Boyajian—now officially known as Boyajian's star and colloquially called Tabby's star—has captivated astronomers and the general public alike. Like all great enigmas, it has generated a seemingly infinite number of possible solutions—none of which wholly explain the curious observations. Whatever is responsible may lie outside the realm of known astronomical phenomena.

UNEARTHED FROM KEPLER'S TREASURE TROVE

BEFORE KEPLER launched in 2009, most planet hunters doggedly revealed new exoplanets (planets orbiting other stars) one by one, like anglers pulling individual fish from the sea. Kepler came along like a trawler, scooping up new worlds thousands at a time.

For four years the telescope continuously observed stars in one small patch of the Milky Way. It was looking for planetary "transits," in which fortuitously aligned worlds cross the face of their host stars and block a fraction of the starlight seen from Earth. Graphed over time, the brightness of a star is described by a so-called light curve. With no transiting planets, the curve will resemble a flat line. Add in a transiting planet, and that light curve will now include U-shaped dips that recur like clockwork each time the orbiting body blocks the star's light. The duration, timing and depth of the dips convey information about the planet itself, such as its size and temperature.

Of the more than 150,000 stars Kepler surveyed, just one—dubbed KIC 8462852, after its number in the Kepler Input Catalog—displayed a light curve that defied explanation. Members of the Planet Hunters citizen science project were the first to notice it when they scoured Kepler's data for transiting worlds overlooked by professional astronomers' automated planet-hunting algorithms. KIC 8462852 showed transitlike dips in starlight seemingly at random, with some lasting a few hours and others persisting for days or weeks. Sometimes the star's light dimmed by about 1 percent (characteristic of the largest transiting exoplanets), but other times it plummeted by up to 20 percent [*see box on page 40*]. No conceivable planetary system could produce such an extreme and variable light curve.

Perplexed, these citizen scientists notified Boyajian, a member of the team overseeing the Planet Hunters project. In 2016 they introduced the star and its mysteries to the world in a peer-reviewed journal article with the subtitle "Where's the Flux?" (Boyajian calls KIC 8462852 the "WTF star").

STRANGE IN MANY WAYS

BOYAJIAN'S STAR held yet more surprises. In the aftermath of her WTF paper, astronomer Bradley Schaefer of Louisiana State University claimed, based on archival data, that Boyajian's star had dimmed by more than 15 percent over the past century.

The claim was controversial because such multidecadal dimming seems next to impossible. Stars stay at nearly the same brightness for billions of years after they are born and only undergo rapid changes just before they die. These "rapid" changes take place on the timescale of millions (rather than billions) of years and are accompanied by clear markers that Boyajian's star

IN BRIEF

KIC 8462852, also known as Boyajian's star, is a strange object discovered more than 1,000 light-years away by the planet-hunting Kepler space telescope.

The star has vexed astronomers with its dramatic and sporadic dimming, a phenomenon difficult to explain via known natural phenomena.

Disks of gas and dust, interstellar debris, comet swarms or even black holes are some of the exotic potential explanations considered by theorists.

Beyond these scenarios is the sensational possibility that the bizarre behavior of Boyajian's star reflects the activities of an advanced cosmic civilization.

lacks. According to every other measurement made, it is an unremarkable middle-aged star. There is no evidence that it is a variable star, pulsing with a regular beat. And there is no indication that it is accreting material from a companion star, no suggestion of anomalous magnetic activity, and no reason to think it might be young and still forming—all phenomena that could rapidly alter its brightness. In fact, aside from its anomalous dimming, this star appears entirely ordinary.

Yet Schaefer's claim held up when astronomers Benjamin T. Montet and Joshua D. Simon checked it with the original, lesser known Kepler calibration data. They found that Boyajian's star faded by 3 percent over the four-year Kepler mission, an effect as extraordinary as the shorter-term dips.

We must now explain two mind-boggling phenomena related to Boyajian's star: slow dimming over at least four years (and possibly the past century) and deep, irregular dips spanning days or weeks. Although astronomers would prefer a single explanation for both, each phenomenon is difficult to explain on its own and even harder to explain when considered in tandem with the other.

MANY ANSWERS, NONE PERSUASIVE

HERE WE CONSIDER some of the most oft-proposed scenarios to explain the bizarre observations of Boyajian's star. We will judge each on how well it explains the observations and offer our subjective assessment of the probability that the theory is correct.

A DISK OF DUST AND GAS

The irregular dips and long-term dimming of Boyajian's star are seen elsewhere—around very young stars with still forming planets. Such stars are belted with circumstellar disks of starlight-warmed gas and dust that, as they form planets, develop clumps, rings and warps. In disks seen edge-on, those features can briefly dim a star's light, and wobbling circumstellar disks can block increasing amounts of a star's light over decades and centuries.

The star is middle-aged, not young, and apparently devoid of a disk. That disk would—as with anything warm—radiate heat as extra infrared radiation, yet Boyajian's star shows no such excess. It could be that the dust and gas exist in a very thin ring sprawled wide around the star, so that the ring blocks starlight along our line of sight without producing much infrared excess. Such rings have never been observed around a middle-aged star such as Boyajian's. Because this scenario can explain Boyajian's star only by invoking a never before seen phenomenon, we judge it to be very unlikely.

A SWARM OF COMETS

Boyajian's original hypothesis was that transiting swarms of giant comets caused the star's dimming. Comets, after all, spend most of their time far from their star and have highly eccentric orbits, which could account for the irregularity of dimming. But what about the lack of heat? The comets would certainly warm up as they approached Boyajian's star and quickly lose that heat as they departed. Any infrared excess would therefore be detectable only during a dip. We detect no infrared excess now, but that absence would make sense if the comets that caused dips a few years ago are now very far from the star, cold and giving off no detectable heat. Even so, any cometary swarm that could also cause the mysterious long-term dimming would have to be very large, unavoidably creating an infrared excess, which, as noted, is missing.

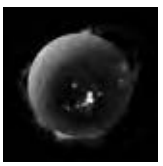
Thus, our verdict is that a cometary explanation is plausible for the dips and very unlikely for the long-term dimming. It stands to reason, though, that if comets are not causing the long-term dimming, then they are probably not causing the dips, either.

A CLOUD IN THE INTERSTELLAR MEDIUM OR SOLAR SYSTEM

Interstellar space is strewn with gas and dust that diminishes starlight. Maybe an intervening cloud or dense sheet of this material blocks a shifting fraction of light as Kepler's line of sight passes through different parts of it during the telescope's orbit around the sun. Such a cloud could have a density gradient that dims Boyajian's star over long timescales, as well as small knots of material that could cause the extreme short-term dips.

This hypothesis finds some support in the work of Valeri Makarov of the U.S. Naval Observatory and his colleague Alexey Goldin. They argue that some of the smaller dips of light attributed to Boyajian's star are actually deep dips in brightness from fainter adjacent stars in Kepler's field of view, possibly caused by swarms of tiny, dense clouds or comets in interstellar space. We subjectively rank this hypothesis to be plausible.

A related hypothesis suggests that the obscuring cloud may be at the outskirts of our own solar system. In that case, Kepler's orbit around the sun would take the craft's line of sight through such a cloud every year, but we see no annual repetition to the dips of Boyajian's star. Furthermore, there is currently no reason to think that such a cloud exists. Although one could conceive of a cloud of ice and vapor arising from geysers on a Pluto-like body much farther out from our sun, until planetary scientists weigh in on this hypothesis, we rate it conceivable but unlikely.



INTRINSIC STELLAR VARIATIONS

Stars do change in brightness when they begin to exhaust the fuel supply in their core. But this happens on timescales of millions of years, not centuries or days, and at the end, not the middle, of a star's life. Naturally occurring phenomena such as star spots and flares, seen often on our sun, change the brightness of stars on shorter timescales. We may not need to invoke additional orbiting material if the irregular dips and long-term dimming can be explained by brightness variations innate to physical processes within Boyajian's star.

Recently Mohammed Sheikh and his colleagues at the University of Illinois at Urbana-Champaign statistically analyzed the timings, depths and durations of the short-term dips, finding that they are distributed according to a "power law" characteristic of a continuous phase transition (such as magnets realigning themselves in the presence of external magnetic fields). They suggested this distribution could hint that the dips of Boyajian's star are caused by its being on the cusp of an internal transition, such as a global flip of its magnetic field.

But no star like Boyajian's has ever displayed such activity. In fact, the star appears too hot to have the type of stellar dynamo

that generates magnetic effects within cooler stars such as our sun. Most problematically, stellar magnetic fields could not create the long-term dimming we see.

Columbia University astronomer Brian Metzger and his colleagues there and at the University of California, Berkeley, have fleshed out a more feasible explanation in which a planet or brown dwarf collided with Boyajian's star. The collision would cause the star to temporarily brighten—and the long-term dimming we see would be the star returning to normal brightness. This scenario does not naturally explain the irregular dips or the detailed shape of the dimming seen by Montet and Simon in the Kepler calibration data, but future studies could solve these problems.

For these reasons, we render a verdict of somewhat plausible for the merger scenario and very unlikely for other explanations invoking intrinsic brightness variations.

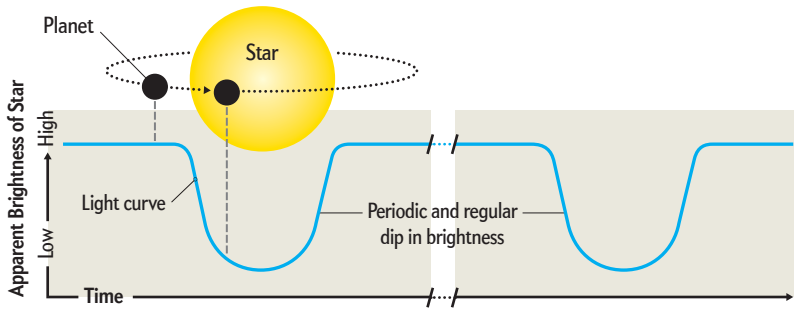
OBSERVATIONS

Enigmatic Light Patterns

To astronomers, there is usually no mystery behind a star fading in the sky. Starspots as well as the shadows of planets or debris disks routinely dim the otherwise steady light from mature stars. But none of these explanations seems to apply for one mercurial middle-aged sun known as KIC 8462852—also called Boyajian's star.

Typical Light Curve

A dimming star can be studied by its light curve—its brightness plotted over time. A planet or disk "transiting" across a star causes a dip in the curve; for planets, this dip recurs every orbital period. Starspots create patterns in light curves based on a star's rotation rate and activity cycle.

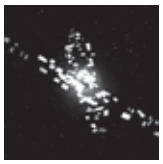


BLACK HOLES

Some members of the public have suggested that a black hole might be involved. One common idea suggests that a stellar-mass black hole in close orbit around Boyajian's star could block the star's light. That hypothesis fails, however, in three ways. First, because such a black hole would tug the star to and fro in the sky, it would create an easily detectable wobble—a wobble that Boyajian's team looked for and did not detect. Second, stellar-mass black holes are far smaller in size than stars, so one of them would block only a minuscule amount of a star's light. In fact, a black hole's intense gravitational field would counterintuitively magnify most of a background star's light rather than blocking it at all. Third, when a black hole consumes gas and dust, it heats the infalling material so much that it glows brightly at all wavelengths. If there really were a black hole between us and Boyajian's star, we would expect a brightening, not dimming, which we definitely do not see. So, no black hole, right?

Well, not quite. A possible solution involves a distant, free-floating black hole drifting between Boyajian's star and us. Imagine that such a black hole is orbited by a wide, cold disk of material—like the rings of Saturn but larger than our entire solar system—and that this disk possesses an almost transparent outer region and a denser inner region. Such a disk could cause the long-term dimming of Boyajian's star as its nearly invisible outer region, followed by its dense inner region, drifted across our line of sight during the past 100 years. The star's irregular dips might then be shadows cast by rings, gaps and other substructures in the transiting disk. Such a black hole (and its hypothetical disk) would have escaped Boyajian's efforts at high-resolution imaging because it would emit no light itself.

Because we lack observational evidence that black holes host cold, sprawling disks at all, this scenario may seem a bit far-fetched. But theorists predict such disks as a by-product of the supernovae that can give birth to stellar-mass black holes. Moreover, statistical estimates do suggest that such a black hole could have passed in front of at least one of the 150,000 stars monitored by Kepler during the four years of its survey. We subjectively rate this theory as somewhat plausible.



ALIEN MEGASTRUCTURES

Having examined a host of natural explanations for the odd behavior of Boyajian's star and found them lacking, we can now consider the most sensational possibility—an alien megastructure, akin to what Dyson described more than half a century ago.

Imagine that an alien civilization built large numbers of energy-collection panels and that the panels had a range of sizes and orbits around the star. The combined effect of the smaller panels of the swarm would be that they blocked some fraction of the light from the star like a translucent screen.

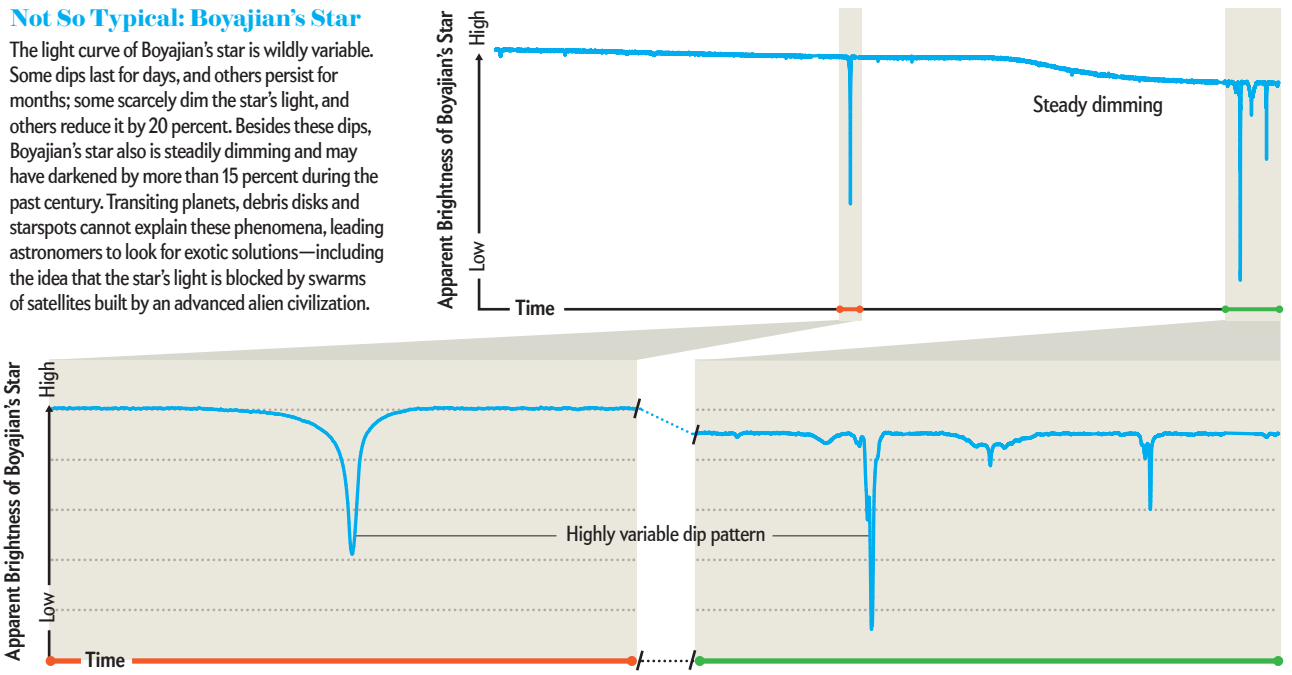
As denser parts of the swarm come into and out of our line of sight, we might see variations in brightness on scales from hours to centuries. As first noted more than a decade ago by astronomer Luc F. A. Arnold, particularly large panels or groups of panels flying in formation—even bigger, perhaps, than the star itself—would cause huge, discrete dips related to their geometric shape as they transited.

As with the circumstellar disk hypothesis, the lack of infrared emission is a problem. Even alien megastructures must obey fundamental physics, so any energy from starlight they intercept must ultimately be radiated away as heat. This requirement holds no matter how efficient their technology is. Energy cannot be destroyed, so if they are collecting a lot, they must also get rid of a lot in the long run.

There are still ways to make the hypothesis work: a megastructure swarm might radiate its gathered energy away as radio or laser signals instead of heat; it might not form a spher-

Not So Typical: Boyajian's Star

The light curve of Boyajian's star is wildly variable. Some dips last for days, and others persist for months; some scarcely dim the star's light, and others reduce it by 20 percent. Besides these dips, Boyajian's star also is steadily dimming and may have darkened by more than 15 percent during the past century. Transiting planets, debris disks and starspots cannot explain these phenomena, leading astronomers to look for exotic solutions—including the idea that the star's light is blocked by swarms of satellites built by an advanced alien civilization.



ical swarm but a ring precisely aligned with our line of sight; it might use technology beyond our understanding of physics that emits no heat at all. Because of the myriad unknowns, this hypothesis is very hard to test.

The alien megastructure hypothesis would have to be considered seriously if all natural hypotheses are ruled out. Alternatively, it would find support if we detected obviously artificial radio signals being transmitted from the vicinity of Boyajian's star—a search we have already begun with Boyajian using the Green Bank Telescope in West Virginia. For now, our verdict on the most sensational hypothesis to explain Boyajian's star is that its plausibility is unclear: we just do not know enough to put even a qualitative probability on the actions of hypothetical alien life.

AN UNKNOWN, BUT BRIGHT, FUTURE

WHERE DOES THIS leave us in trying to understand Boyajian's star?

We can rule out any explanation that requires an excess of infrared energy because it is not observed. We can also reject scenarios that require many low-probability events or that invoke physics or objects we have never seen before—at least until all other options have been eliminated.

The best path forward is more fact-finding. Boyajian, now an assistant professor at Louisiana State University, leveraged the public fascination with this star into a successful crowdfunding campaign that purchased time for us on the Las Cumbres Observatory Global Telescope network. We monitor the star multiple times a day, and if its light dips again, we have several telescopes ready to swing into action to measure the spectrum of the missing light, which will tell us the composition of the intervening material.

Other astronomers are seeking out additional archival measurements of the star's brightness to learn more about its long-term dimming. Knowing the timescale of the dimming would further constrain theories about the star's odd light curve and improve our knowledge of how to search for more observational clues.

We also await a better measurement of the distance to Boyajian's star—due from the European Space Agency's Gaia mission—which should help eliminate some hypotheses. If the star is closer than 1,300 light-years, extinction from gas and dust in the interstellar medium cannot explain the current level of dimming. If instead the distance is about 1,500 light-years (the current best estimate), the long-term dimming could perhaps be because of chance patterns of intervening dust along the line of sight. But if the star is much farther away than that, it is far more luminous than previously believed—and then the dimming could be a return to normalcy after a merger, as Metzger's team has suggested.

Unless and until more information trickles in from measurements with the Green Bank Telescope, Las Cumbres Observatory and Gaia, our speculations about Boyajian's star are only limited by our imagination and a healthy dose of physics. Like the best puzzles in nature, the journey to the truth behind this enigmatic star is far from over. SA

SOURCE: "KIC 8462852 FADED THROUGHOUT THE *KEPLER* MISSION," BY BENJAMIN T. MONTET AND JOSHUA D. SIMON, IN *ASTROPHYSICAL JOURNAL LETTERS*, VOL. 830, NO. 2, ARTICLE NO. L39; OCTOBER 20, 2016

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scientificamerican.com/magazine/sa

Graphic by Tiffany Farrant-Gonzalez

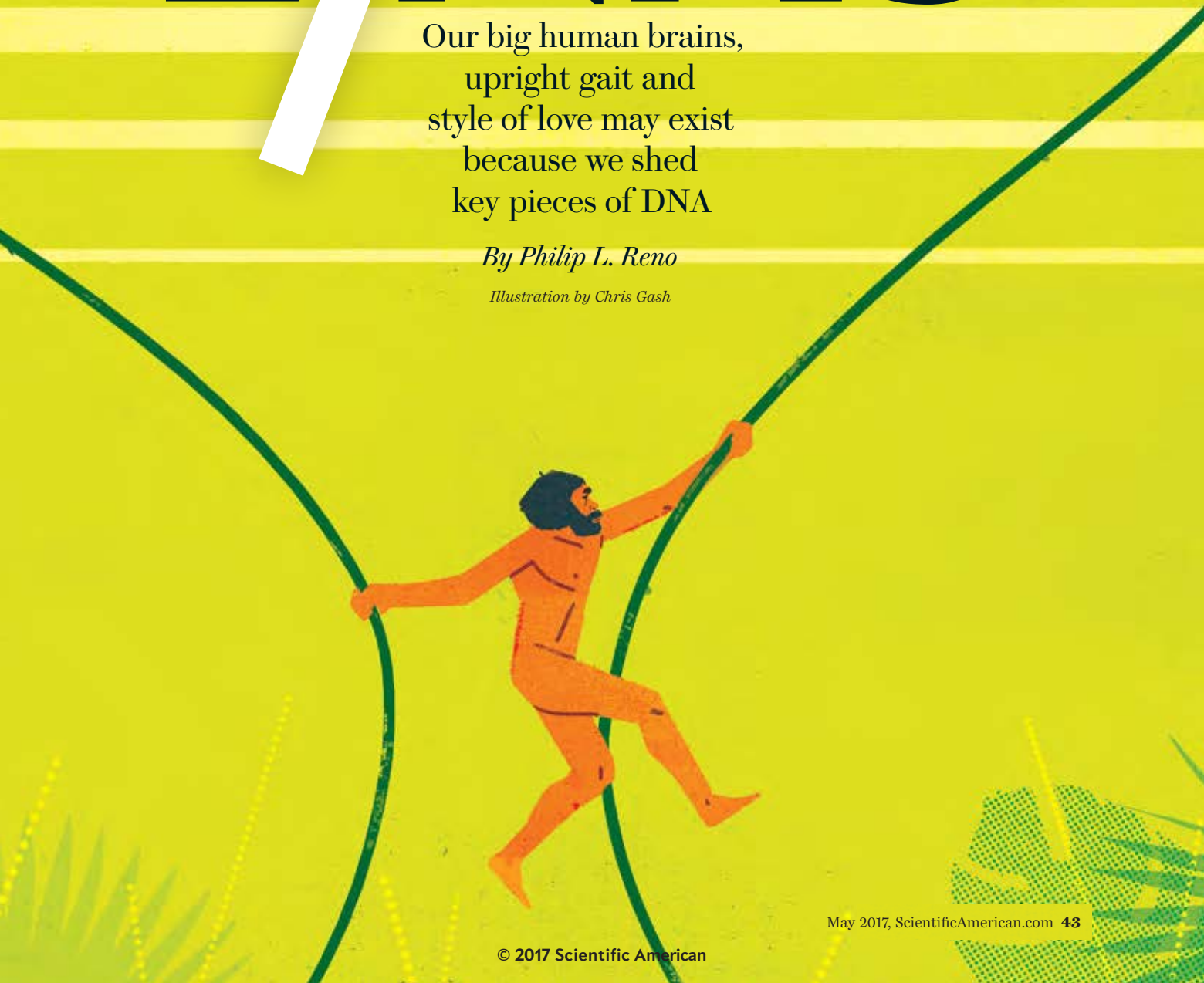
EVOLUTION

MISSING LINKS

Our big human brains, upright gait and style of love may exist because we shed key pieces of DNA

By Philip L. Reno

Illustration by Chris Gash



Philip L. Reno is an associate professor of biomedical sciences at the Philadelphia College of Osteopathic Medicine.

WHEN WE VISIT A ZOO AND PEER AT OUR CLOSEST LIVING RELATIVES, the great apes, two things reliably captivate us. One: they look so very much like people. The expressive faces and the grasping hands of chimpanzees, bonobos, orangutans and gorillas are eerily similar to our own.

The other: these creatures are so clearly *not* us. Our upright walking, capacious and clever brains, and a list of other traits sharply set us apart. What were the key defining events in evolution that make us uniquely human? Why did they happen—and how? Anthropologists and evolutionary biologists have toiled at such questions for decades and increasingly are turning to modern genetic technologies to help crack the mystery. We have found that some of the most important human characteristics—features that set us apart from our closest relatives—may have come not from additions to our genes, as one might expect. Instead they have come out of losses: the disappearance of key stretches of DNA.

Several research laboratories, including mine, have traced some of this lost DNA across time, comparing human genomes with those of other mammals and even archaic humans: the Neandertals and our lesser known cousins, the Denisovans. We have learned that during the roughly eight million years since our lineage split from chimps, our ancestors' genomes were stripped of DNA "switches" that activate key genes during development. Neandertals share our loss, making it clear the vanishing act occurred early in our evolutionary path.

In fact, loss of these DNA sequences appears to be linked to quintessentially human traits: big brains, upright walking and our distinctive mating habits. (The last part of the project led me, in the course of my experiments, to learn a surprising amount about the structure of primate penises.)

LOSERS

I FIRST DEVELOPED A KEEN INTEREST in human evolution during my Ph.D. years with noted anthropologist C. Owen Lovejoy of Kent State University, where I studied the difference in skeletons of males and females in extinct human relatives. I wanted to continue this kind of work to learn what, in our genes and developmental processes, had changed as humans progressed along our unusual evolutionary path. I was fortunate to obtain a postdoctoral position with David Kingsley of Stanford University, who was bearing down on just the kind of questions that fascinated me.

Among other work, Kingsley's lab had identified DNA changes involved in the evolution of stickleback fishes—including the deletion of a stretch of DNA in freshwater sticklebacks that, it turned out, caused the spiny pelvic fins to be lost in those species. That lost DNA piece contained a "switch" that was needed to activate a gene involved in pelvic spine development, at the right time and place.

If this kind of process had happened in sticklebacks, why not in human beings, too? It seemed reasonable to suppose that subtle changes in when and where genes are turned on during development might be one way our genome had evolved to generate our unique anatomy.

Inspired by that fishy example, we set out to see if we could find important switches that had disappeared in human beings over evolutionary time. Today's availability of completely sequenced human and ape genomes, as well as the computation-

IN BRIEF

Recent analyses have identified more than 500 stretches of DNA that were lost from the human genome but still exist in chimpanzees and other mammals.

Three stretches appear to be DNA switches, and loss of two of them freed brains to grow and humans to evolve pair bonding with mates.

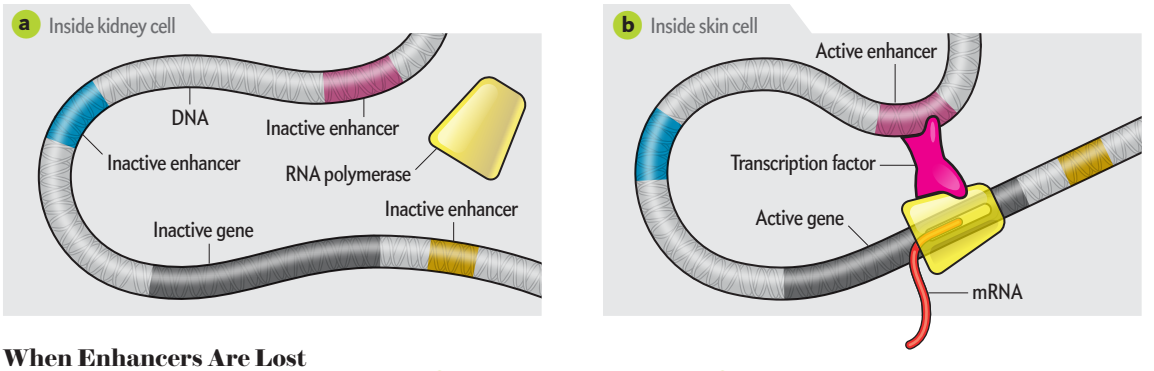
Loss of another switch from our ancestors may have refined our upright gait, which freed our hands to make and carry tools.

Gene Turn-ons and Turnoffs

Not all human genes are active in all cells or at all times. The different activity patterns are key to the growth and function of different body parts. DNA on-switches called enhancers help to control the patterns, and a single gene may be affected by multiple enhancers that change the gene's effects in different places. Switches present in other animals, but lost in us, may have produced unique human traits.

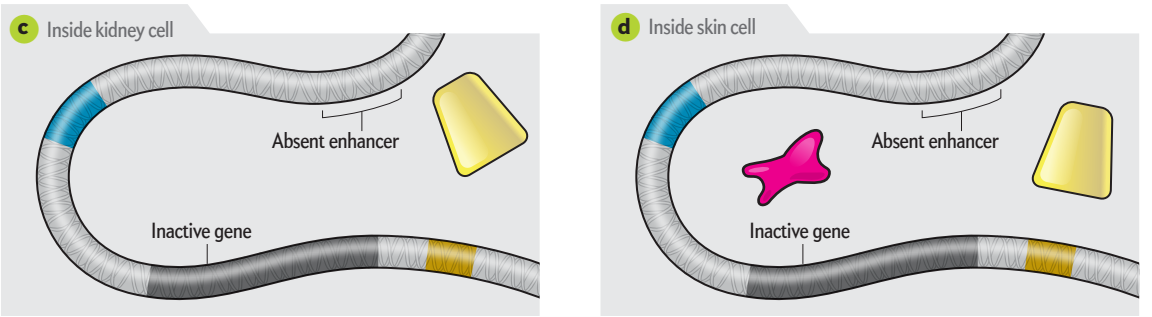
How Enhancers Affect Cells

One gene could be controlled by three enhancers, active in different ways in a kidney cell **a** and a skin cell **b**. The kidney cell does not produce a molecule, called a transcription factor, that is needed to activate the enhancers and to use an important enzyme, RNA polymerase (*yellow*), which reads the gene's code. The skin cell, in contrast, does produce one transcription factor (*pink*) that binds to the pink enhancer. This activates the gene, producing an mRNA molecule (*red*) that conveys the gene's instructions to the cell.



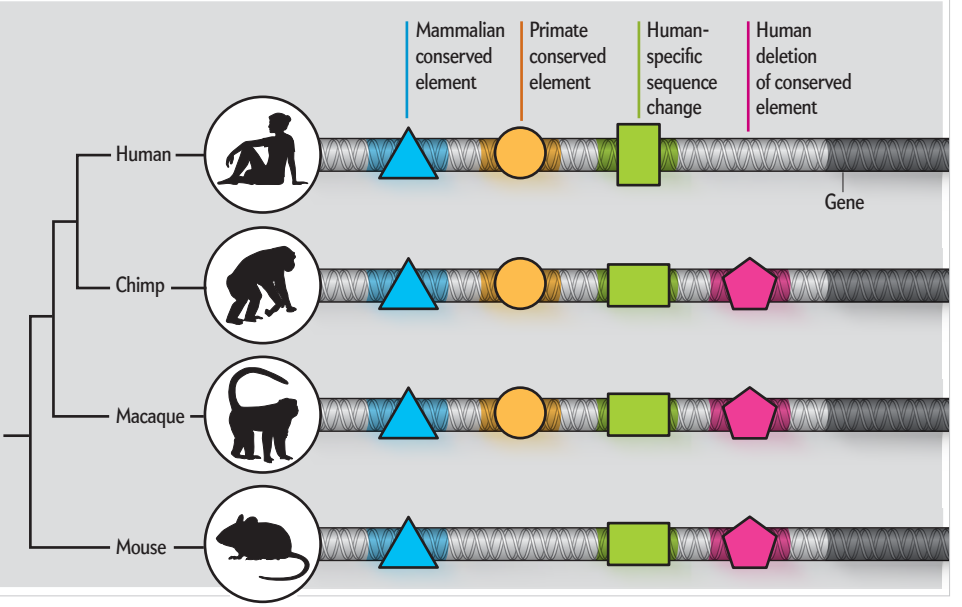
When Enhancers Are Lost

If the pink enhancer is absent, the gene in the kidney cell **c** is still inactive. But in the skin cell **d**, the formerly active gene is now off and does not send instructions to the cell. (In other cell types, activity affected by the other two enhancers would continue.)



Our Missing Switches

Stretches of nonprotein-coding DNA hold elements like switches. Scientists compared such stretches in chimps, humans, macaques and mice to find switches in other animals that had vanished by the time humans evolved. In some cases (*triangles*), the DNA elements were present in all species, suggesting they were important to all the mammals. In other cases (*circles*), primates had the elements, but mice did not, implying the elements were important only to the primate lineage. A few elements (*rectangles*) had unique changes in humans that may have been important for our evolution. And some elements (*pentagons*) were present in mice, chimps and macaques—but missing in humans. These lost regions could contribute to the traits that make us different.

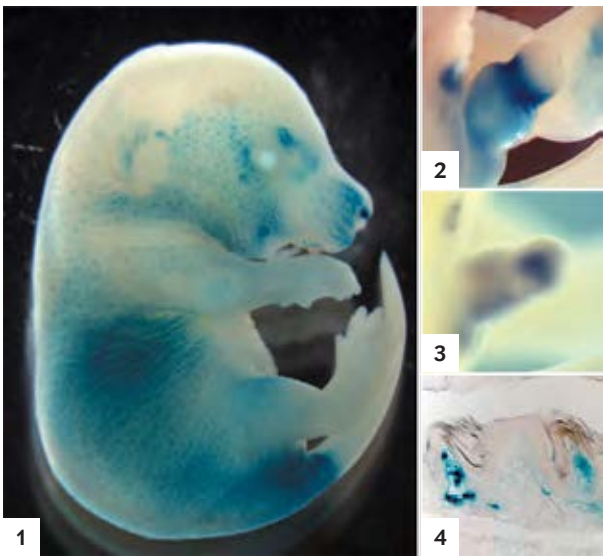


Graphic by Jen Christiansen

al tools needed to analyze them, made our experiments possible. A group of us in Kingsley's lab teamed up with Stanford computational scientist Gill Bejerano and then graduate student Cory McLean to plan the experiments.

Finding missing switches is not easy, because genomes are vast. Ours contains 3.2 billion bases (the individual letters of a DNA sequence), and about 100 million of these differ between humans and chimps. How could our experiment be done? To understand our approach, a bit of background is in order.

We know that in a creature's genome, stretches of DNA that are doing important jobs are preserved during evolution with high fidelity. We also know that the more closely related two species are, the more similar their genetic sequences will be. In the case of chimps and humans, for example, our genomes are 99 percent identical in the tiny portion—less than 1 percent—that carries instructions for making proteins. And they are 96 percent identical in the much larger portion of the genome that does not contain these protein-coding genes.



MOUSE TEST: To see what a genetic switch did, scientists injected it into mouse embryos with DNA that turned cells blue where the switch was "on." Blue showed up in spots that develop into sensory whiskers and other hair follicles (*1*) and cells that form the penis or clitoris and mammary glands (*2*). Other techniques showed the switch is very near a gene that lets cells respond to sex hormones such as testosterone (*3*), and in adult male mice the switch is very active in cells that create penile spines (*4*).

COURTESY OF PHILIP L. RENO

SEARCHING THE JUNK PILE

WE WERE INTERESTED in this much larger area—stretches that, in the past, were written off as "junk" DNA but are now known to be stuffed with switches that turn genes on and off. The work of these switches is crucial. Although pretty much all human body cells contain the same 20,000 or so genes, they are not all turned on everywhere or at all times and places. Only certain genes are needed to build a brain, for example, and others for bones or hair. Because chimps and humans, despite their differences, have the same basic bodily structure, it is not surprising that the vast, switch-containing terrain in our genomes has a lot of similarities.

The differences were what mattered to us. Specifically, we wanted to find sequences that had been preserved across evolutionary time in many species (indicating that the sequences were important) but were no longer present in humans. To do this, our computational genomics collaborators first compared the chimpanzee, macaque and mouse genomes. They pinpointed hundreds of DNA chunks that remained nearly unchanged among all three species. The next step was to scour this list to find chunks that did not exist in the human genome and thus had been lost sometime after our lineage diverged from the chimp's. We found more than 500.

Which of them to study? Because we wanted to find switches that might alter mammalian development, we focused on deletions near genes with known roles in that process. One of my colleagues pursued a deletion near a gene that regulates formation of neurons; another worked on a deletion near a gene involved in skeletal formation.

For my part, because of my interest in the evolution of the differences in male and female body forms, I was excited by a deletion near the gene for the androgen receptor. Androgens such as testosterone are hormones needed for the development of male-specific traits. Made in the testes, they circulate through the bloodstream. In response, cells that actively make androgen receptors will then follow a male pattern of development: formation of a penis instead of a clitoris, for example, or (later in life) beard growth and an enlarged larynx for a deep voice.

We needed, first, to test if those chunks of DNA really contained on-switches. To do this, we extracted them from both chimp and mouse DNA and attached them to a gene that turns cells blue—but only when that gene is activated. We injected this stitched-together piece of DNA into fertilized mouse eggs to see if any parts of the embryos were blue as they developed—indicating a functional switch in the piece of DNA—and, if so, where.

MALE TURNOFFS

MY RESULTS WERE EXCITING: they really seemed to show that I was working with a true on-switch for the androgen receptor, one that human beings had shed. In mouse embryos, the genital tubercle (which develops into either a clitoris or penis) stained blue, as did the developing mammary glands and spots on the mouse face where sensory whiskers called vibrissae form. All these tissues are known to make the androgen receptor respond to testosterone. Looking more closely, I saw that the staining on the developing genitals was situated in places where small, tough protein spikes later form on the mouse penis.

Neither sensory whiskers or spiny penises are human features, of course. But they occur in many mammals, including mice, monkeys and chimps. It is also known that a loss of testosterone results in shorter whiskers in male rodents and a lack of penile spines in rodents and primates. Penile spines and whiskers might similarly disappear if a crucial DNA switch were lost and the androgen receptor were no longer made in these tissues.

As I pursued my experiments, others were busy with their own deletions of choice, with intriguing results as well. Then graduate student Alex Pollen found that his chunk of DNA activated the neural gene it was near, at precise spots in the devel-

Loss of penile spines, we believe, is one of the changes that had far-reaching effects on our evolutionary path.

oping brain. The gene is involved in a key process: it helps to kill off surplus neurons, which are overproduced during embryonic development. That offers a tantalizing thought: because the human brain is far larger than the chimp's (1,400 versus 400 cubic centimeters), might loss of this switch have contributed to that evolutionary ramp-up, by releasing brakes on brain growth?

Vahan B. Indjeian, then a postdoc in the lab, similarly found that his switch turned on the gene involved in skeletal growth—in developing hind limbs, specifically the toes of the foot. Toes two through five in humans are shorter than in apes and mice, alterations that improve the foot for upright walking.

It is easy to see how brain and bone switches fit into the pattern of human evolution. Loss of both appears linked to hallmarks of humanity: a big brain and walking on two legs. Loss of sensory whiskers is fairly easy to rationalize because we no longer root around in the dark with snouts to grub out food or capture prey but use hands, in daylight, to find nourishment. Despite their reduced importance, though, it is unclear how we would be better off without these whiskers.

SENSITIVE RELATIONSHIPS

THE PENILE SPINE STORY is less intuitive, but it is potentially more powerful and also fits neatly into the adaptive history of our species. Loss of spines, we believe, is one of a suite of changes that together had far-reaching effects on our evolutionary path. Together these changes altered the ways we mate, the physical appearance of males and females, our relationships with one another and the ways we care for offspring.

Made of keratin, the same stuff as our fingernails, these spines occur in many mammals, including primates, rodents, cats, bats and opossums, and range from simple microscopic cones to large barbs and multipronged spikes. They may serve varied functions depending on the species: heightening stimulation, inducing ovulation, removing sperm deposited by other males, or irritating the vaginal lining to limit female interest in mating with others.

The copulation time of spine-sporting primates is remarkably brief: in the chimp, typically less than 10 seconds. And historical experiments in primates show that removal of penile spines can extend copulation by two thirds. From such observations we can surmise that loss of penile spines was one of the changes in humans that have made the sex act last longer, and thus be more intimate, compared with that of our spine-bearing forebears. That sounds pleasant, but it could also serve our species from an evolutionary perspective.

Our own reproductive strategy is unlike that of any apes, which all have intense male-male competition at their core. In chimps and bonobos, males compete to mate with as many fertile females as possible. They produce copious quantities of sperm (chimp testicles are three times larger than human ones), have penile spines and, like all male great apes and monkeys, have deadly, fanglike canines to discourage rivals. They leave rearing of offspring entirely to the female. Thus, for her, successful mating results in considerable commitment—gestating, nursing and rearing each infant to independence—and the female does not reproduce again until the weaning is completed.

Humans are different. They form fairly faithful pair bonds. Men often help to rear offspring, enabling earlier weaning and increasing reproductive rate. Male-male competition is not as intense. We believe that loss of penile spines went along with loss of other traits associated with fierce competition (such as dangerous canines) and gain of others that promote bonding and cooperation.

Bipedalism, as Lovejoy proposed, could be one of these features. Early male help probably initially took the form of procuring foods rich in fat and proteins, such as grubs, insects and small vertebrates, that required extensive search and transport. Males would need to travel far with hands free for carrying, which likely provided the initial selective advantage for walking on two legs.

GENE LOSS AND FEATURE GAINS

AND THERE IS MORE. Cooperation and provisioning would also allow parents to rear dependent offspring for longer and thus lengthen the juvenile period after weaning. This would offer a longer time for learning and therefore enhance the usefulness of a large, agile brain—indeed, perhaps set the stage for its evolution.

In that sense, the individual stories of all three of our deletions are deeply intertwined.

When I came to Kingsley's lab, I did not anticipate the turn my work would take—that I would find myself poring over fusty 1940s texts on mammalian genital structure. My lab is continuing research into this and other genetic and developmental changes with big consequences: the evolutionary shaping of the delicate bones in the human wrist to perfect them for toolmaking.

There is much we may never know about all this distant history, no matter how keen we may be to find out. But even if we cannot be sure about the why of an evolutionary change, with the tools of modern molecular biology we can now tackle the how—a critical and fascinating question in its own right. SA

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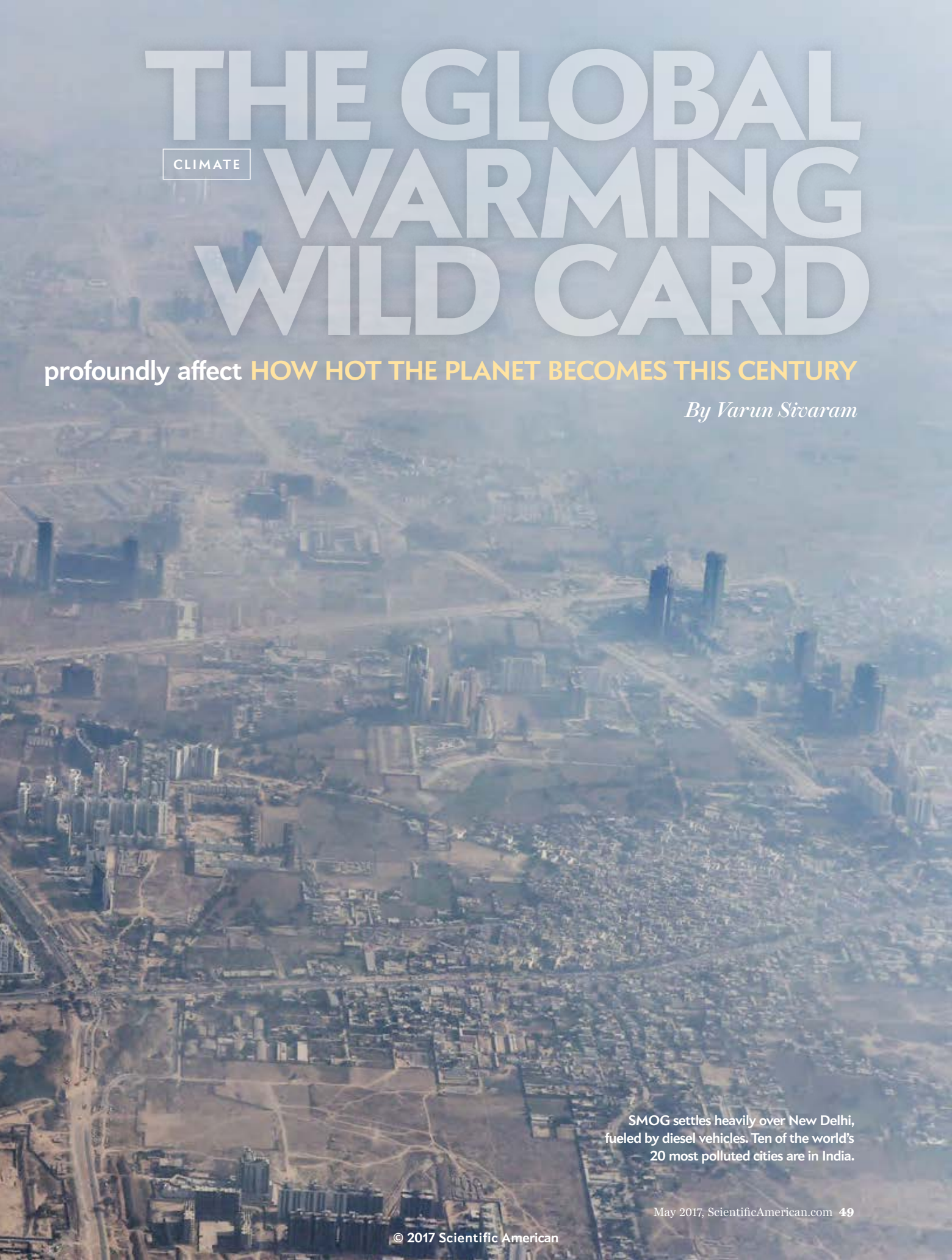
Energy decisions that INDIA makes in the next few years could

CLIMATE

THE GLOBAL WARMING WILD CARD

profoundly affect HOW HOT THE PLANET BECOMES THIS CENTURY

By Varun Sivaram



SMOG settles heavily over New Delhi, fueled by diesel vehicles. Ten of the world's 20 most polluted cities are in India.

Varun Sivaram is a fellow at the Council on Foreign Relations and acting director of its Program on Energy Security and Climate Change. He is also an adjunct professor at Georgetown University. Sivaram co-wrote our July 2015 feature on how perovskites could overtake silicon materials for solar power.

A SHIMMERING WATERFALL BECKONED VISITORS INTO the India pavilion at the 2015 Paris Climate Change Conference. Inside, multimedia exhibits and a parade of panelists proclaimed that the nation's clean energy future was fast-approaching. Prime Minister Narendra Modi went even further, announcing that his country would lead a new International Solar Alliance to ramp up solar power in 120 countries. Indian officials resolved to be leaders in battling global climate change.

I had arrived in Paris after a research trip that crisscrossed India, and I struggled to square that confident optimism with the facts I had seen on the ground: heavy reliance on coal power plants, a failing electrical grid that could not handle large additions of wind or solar electricity, and a widespread attitude that India, as a developing country, should not have to reduce its carbon emissions and should be able to grow using fossil fuels as other major countries have done. Still, by the end of the conference, India and 194 other countries, along with the European Union, had adopted the Paris Agreement, which commits the world to limit global warming to two degrees Celsius. In November 2016 the agreement went into legal force, making each country's pledge binding under international law.

Despite the lofty rhetoric of India's leaders, their vision of a clean energy future is far from assured. Even though India's pledge set ambitious targets for solar and wind power, its overall commitment to curb emissions was underwhelming. If the government just sat on its hands, emissions would rise rapidly yet stay within the sky-high limits the country set for itself in Paris.

That would be disastrous for the world. India has one of the fastest-growing major economies on the planet, with a population expected to rise to 1.6 billion by 2040. By that time, electricity demand could quadruple. If the nation does not take drastic measures, by midcentury it could well be the largest greenhouse gas emitter (it is third now, behind China and the U.S.), locked into a fossil-fuel infrastructure that would likely ruin the world's quest to contain climate change. If it adds coal power at the rate needed to keep up with its skyrocketing demand, for example, its greenhouse gas emissions could double by 2040.

Yet India is in some ways starting with a clean slate. Unlike the developed world, where the challenge is replacing dirty fossil-fuel infrastructure with clean energy, most of India's infrastructure has not been built yet. The country has a choice to invest in power from wind, solar and natural gas rather than coal. And more efficient appliances, factories and vehicles could rein in demand, making it easier to switch to cleaner sources. Recently the government has hinted that it might improve on its disappointing Paris pledge. But for now the energy juggernaut is just plowing ahead. What would it take to get India onto the cleaner path? Which decisions could doom the planet?

MORE POWER FOR ALL

PRIMITIVE AND DIRTY SOURCES dominate India's energy mix. Two thirds of households continue to rely on cow dung patties, straw, charcoal and firewood for cooking and heating—nearly a quarter of the nation's primary energy supply. Almost all the rest comes from coal and oil. Coal-fired power plants generate three quarters of India's electricity, and half of the country's industries burn coal to generate heat needed for processes such as steelmaking. Oil drives nearly the entire transportation sector.

These fossil fuels are nominally cheap, but they exact a heavy toll. In addition to climate change, they contribute to urban smog; 10 of the 20 most polluted cities in the world are in India. Coal plants consume large volumes of water. And growing reliance on foreign coal and oil imports causes economic insecurity; India's currency has suffered rapid devaluations during global oil crises.

The most promising route to modern and clean energy runs through the electric power sector. As costs fall, renewable sources of electricity are increasingly cost-competitive with coal. Down the road, electricity could power scooters, cars and trucks, loosening oil's stranglehold on transportation.

None of this is easy. The grid does not even reach more than 300 million Indians. Millions more who are within reach lack reliable power because the grid is in shambles—and certainly in no

IN BRIEF

India's population and living standards have been rising quickly. If its current energy mix continues, by 2040 carbon emissions would prevent the world from limiting global warming to desired levels. **To cut emissions,** India has to build a reliable electrical grid that can handle widespread solar and wind power and that can switch from coal to natural gas power plants.

The country also needs to reform the bankrupt power sector, pass stronger energy-efficiency regulations and invest in clean transportation. Technical and financial assistance from abroad will be crucial.

PRECEDING PAGES: ROBERTO SCHMIDT *Getty Images*; THIS PAGE: JONAS GRATZER *Getty Images*

FIRES ignited by cigarettes, lightning or spontaneous combustion have been burning for decades at the immense Jharia coal strip mines, relentlessly releasing toxic gases and carbon dioxide.

condition to accept an influx of energy from solar or wind technology. In my pre-Paris journey, for instance, I watched terrible storms leave thousands of people without electricity for weeks.

Despite this reality, the Modi administration has laid out a promising vision. In Paris, it pledged to increase the share of nonfossil-fueled electricity to 40 percent by 2030, up from 24 percent today. It went further in late 2016, increasing its forecast to 60 percent, a truly ambitious goal. Hydropower accounts for most of India's nonfossil-fueled electricity today, but difficulties in obtaining permits, acquiring land and negotiating compensation for local communities displaced by dams tend to doom most proposed hydroelectric plants. Chronic construction delays also rule out a major role for nuclear reactors.

To meet its 60 percent target, the government's biggest intention by far is to expand solar and wind to 350 gigawatts by 2030. Of this, 250 GW would come from solar, which would exceed 80 percent of all solar capacity currently in existence around the world. Though ambitious, this target is increasingly realistic thanks to the plunging cost of solar power, which in India has dropped by two thirds in the past five years. A new solar plant is now cheaper than a new coal plant that burns imported coal, and by 2020 solar will be cheaper than new coal plants that use domestic coal. Finally, the government and foreign donors are investing in a national network of transmission lines called green corridors that connect sunny areas such as the Thar Desert in the state of Rajasthan to far-off cities such as Mumbai and Delhi.

The government has also set ambitious targets to deploy solar power on urban rooftops as well as in far-flung villages that the grid does not reach. Indians are fond of pointing out that the telecommunications industry was able to "leapfrog" from very little landline infrastructure to a widespread mobile phone network. By analogy, they argue, India should be able to leapfrog the lack of a fully deployed power grid and adopt local solar power that does not need a national grid. Indeed, the amount of rooftop solar has almost doubled in each of the past four years.

That may be, but large solar energy farms are much cheaper, and a comprehensive grid can power modern appliances well beyond the few lightbulbs and ceiling fan that a typical remote solar installation might support. All this suggests that the best strategy is to pursue both centralized and decentralized power at the same time and to extend and upgrade the grid. Meanwhile distributed solar panels and batteries, especially when networked together as a microgrid that can serve a neighborhood, hospital or data center, can make the entire system more resilient.

THE NATURAL GAS FIX

STILL, POWER DEMAND will grow faster than firms can build renewable energy. And more controllable power sources are needed to buffer the unpredictable output of rising wind and solar generation. For now battery storage is too expensive to deploy at scale.

Natural gas–fired plants could solve both challenges. In the U.S., carbon dioxide emissions from energy have declined roughly 15 percent over the past decade, mostly because gas—half as carbon-intensive as coal—has been replacing coal. Natural gas generates only 8 percent of India's electricity because domestic production is minimal, imported gas has been expensive and prior governments have preferred to rely on domestically abundant coal. But global supplies of liquefied natural gas are rising—from Australia, Africa, even the U.S.—so prices in Asia are falling rapidly.

Gas plants are cheaper and quicker to build than coal plants are, and they can ramp their output up and down to offset variable wind and solar. Natural gas could also displace coal and oil for heat in industry and buildings and even as fuel for transportation, further reducing emissions. Vikram Singh Mehta, chair of Brookings India and former head of Shell India, maintains that India's energy policy should emphasize natural gas infrastructure. India would need to invest heavily in a domestic pipeline network to transport gas and in regasification terminals to import liquefied natural gas.

The Modi administration may be listening. It recently promised that neither the government nor the private sector would build any coal plants after 2022. Modi also pledged to use more natural gas. Keeping the latter promise could ensure the former comes true as well.

USE IT AND LOSE IT

EVEN WITH A MOVE TOWARD renewables and natural gas, coal and oil will dominate India's energy mix in the near term. That is why Navroz Dubash of the Center for Policy Research in New Delhi ar-

gues that more investment in an energy-efficient economy is critical. If India becomes as efficient as some would like, it could be a shining example of a developing country that achieves economic growth without commensurate increases in energy demand, halting the rise in emissions.

Although the International Energy Agency forecasts that by 2040 India, if left unchecked, will need to deliver four times as much electricity as it does now, an aggressive efficiency push could limit the increase to just twice current levels. Making manufacturing facilities more efficient could have a profound effect. Industry currently consumes more than 40 percent of India's energy. Converting to efficient equipment and switching from coal to natural gas or electricity for manufacturing steel, bricks and fertilizer alone could save enormous amounts of energy and emissions.

The country's buildings present another great opportunity. A staggering three quarters of the structures that will be standing in 2040 have not been erected yet. Electricity for homes and businesses could spike, especially as air-conditioning spreads, so it is imperative that India's new buildings use electricity economically.

India is already a leader in using public policy to drive down the cost of energy-efficient products. A recent initiative—Energy Efficiency Services Limited, which procures equipment in bulk and distributes it at low prices—has succeeded wildly. The initiative has sold more than 200 million highly efficient LED lamps at comparable cost to conventional incandescent lightbulbs, and it has driven LED prices down below those in the West. The initiative is beginning to place orders for efficient air conditioners to spur manufacturers to innovate. If this mechanism continues to succeed, the market will drive investment in better appliances as millions of new middle-class Indians demand modern services.

India could also counter rising emissions from transportation. Right now transport consumes only 14 percent of the nation's energy because very few Indians own a car. Fuel demand could more than triple by 2040, however, spurred by rising incomes and greater desire for vehicles. Policy makers recently mandated that new vehicles be increasingly fuel-efficient. But the country could aggressively invest in charging infrastructure to make electric vehicles more attractive, helping renewable power to reduce vehicle emissions. Given that two- and three-wheelers make up more than 80 percent of India's vehicle sales today, the government could make rapid inroads toward electrification by promoting electric scooters and rickshaws in the near term. And if urban planners can deploy effective public transit, they could reduce people's desire to own cars.

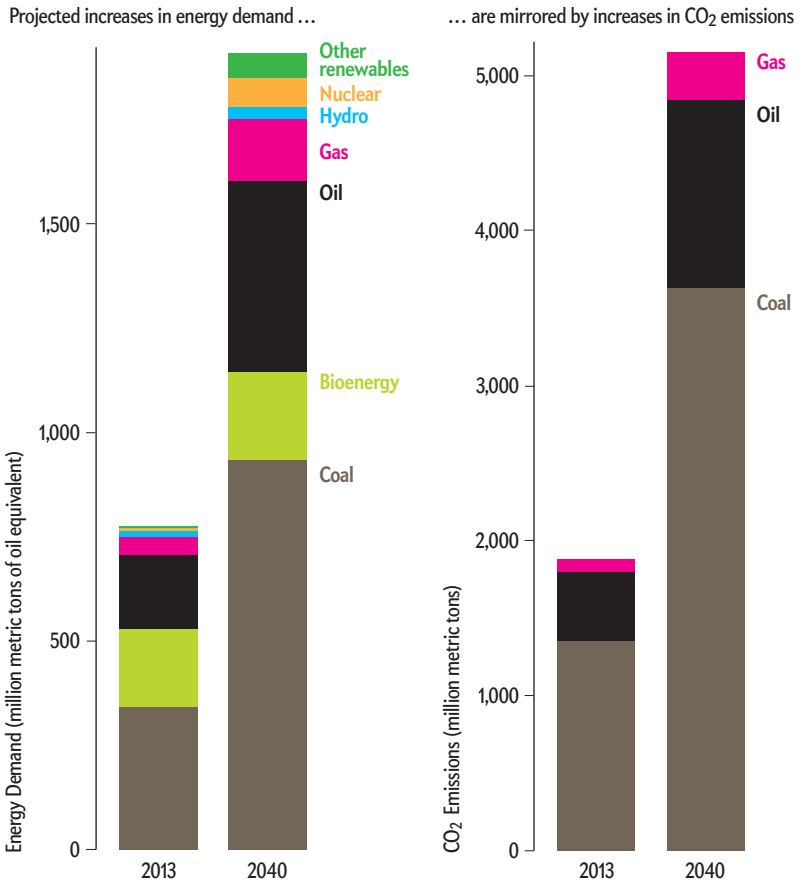
Better transportation in cities could save millions of lives, too. In India, smog and particulate air pollution—largely spewed by diesel vehicles—choke major cities such as Delhi, cost $18 billion annually in lower economic productivity and contribute to more than one million premature deaths every year.

Harnessing solar energy could help relieve strained food and water systems as well. A pilot project in southern India will use concentrating solar mirrors to generate steam, which will drive turbines and distill water and run food refrigeration. The government is also aggressively deploying solar panels to power 200,000 irrigation pumps by 2019, en route to ultimately converting all 26 million pumps—which run on diesel fuel or the power grid—to solar power.

FORECAST

Energy and Emissions Rise

If India's population and economy grow as projected by 2040, energy demand could more than double. And if the country's policies continue to reflect its 2015 Paris pledge, its energy mix will change slowly and carbon emissions could also more than double. Expanding natural gas and solar and wind power, switching to electric vehicles and improving efficiency could more rapidly alter the mix and lessen emissions.



SOURCE: *INDIA ENERGY OUTLOOK: WORLD ENERGY OUTLOOK SPECIAL REPORT*. ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT/INTERNATIONAL ENERGY AGENCY, 2015

REALITY CHECK

IN MY CONVERSATIONS with foreign and domestic companies, especially in the solar sector, I have been struck by a stark contrast. Companies outside India see a lucrative market that will grow at record-breaking pace. But leaders of companies inside

SCIENTIFIC AMERICAN ONLINE More on India's solar power plants is at ScientificAmerican.com/may2017/sivaram

Graphic by Jen Christiansen

India privately scoff. Their pessimism stems from their experience with India's dysfunctional power sector, the lack of funding for infrastructure projects, and the contentious and at times corrupt political landscape. Quintessentially Indian obstacles block easy execution of a clean energy strategy.

First, as noted, the dilapidated power grid is woefully unprepared to handle even a small rise in renewable sources, and that strain will only get worse. For example, as climate change increases drought, farmers are turning on more irrigation pumps that dive deeper belowground and, in so doing, are using more electricity. In 2012 a massive increase in pumping caused the largest blackout in human history. Already bankrupt utilities cannot afford to upgrade the ailing grid, stuck in a vicious cycle of undercharging customers for electricity, going into debt, and failing to maintain the grid or to combat rampant power theft.

MICROGRIDS can power villages that electric transmission lines do not reach. Solar panels feed a local microgrid in one village (*1*). Batteries store solar power for another microgrid (*2*).

PRASHANTH VISHWANATHAN *Getty Images*

Second, erecting infrastructure is notoriously problematic because of scarce private financing and cumbersome regulation. This is troubling because meeting India's renewable energy targets alone will require $150 billion in investment by 2020—far more than the government can mobilize. Again, a vicious cycle has emerged, in which banks have lent heavily to projects that have stalled (especially in the power sector) and are therefore not in good shape to invest further. They often charge exorbitant interest rates. And elusive government permits and obstacles to land acquisition can delay or doom clean energy projects.

Third, governance and its thorny politics can impede sensible policies. For example, even though the Modi administration has set ambitious wind and solar energy targets, implementation rests mostly with the states, many of which have been reluctant to act. Another Modi initiative—to repeal wasteful subsidies for consumer fuels—succeeded in raising the prices of gasoline and diesel but has stalled on raising cooking gas and kerosene prices because of political backlash. And as long as natural gas is sold below market prices, companies have little incentive to invest in drilling new wells to increase domestic production.

Finally, the Modi administration's tax on coal-mining companies has raised the ire not only of coal firms but also of their customers, such as steel companies, and the governments of major coal-producing states. These powerful political forces could obstruct further increases to the tax, which is currently much lower than the cost of the pollution caused by burning coal.

Strong policy changes are needed. A top priority is to rescue utilities from their backbreaking debt so they can reinforce the grid and pay for renewable energy. The Modi administration has made some progress by promising to pay off debts in return for better utility performance, such as lessening power losses in the grid, which can exceed a quarter of the power that goes into them. The administration could go further by reducing state government influence over utilities so the companies are not pressured to reduce rates for politicians' gains. Another priority is to tighten efficiency regulations for industry. And policy makers could fast-track permits for natural gas pipelines and power plants, as well as facilities that import liquefied natural gas. They also could step up incentives for capturing carbon emissions from burning coal, as one chemical plant in southern India recently started doing. Better yet, they could move up the date beyond which no new coal plants will be built to earlier than 2022. All of this will require partnerships between the federal and state governments, as well as political courage against industry lobbies. The most effective way to build a political coalition is to make the clean energy infrastructure financially attractive, which initiatives such as Energy Efficiency Services Limited have done by encouraging local manufacturing.

HELP FROM ABROAD

INDIA WILL NOT ACHIEVE a low-carbon transition alone. It will need help developing new technologies and financing their deployment. Some signs are encouraging: India has partnerships with the U.S. on clean energy research and development, with Germany on financing grid infrastructure and with multilateral development banks on deploying renewable energy.

The scale of assistance will need to increase by at least an order of magnitude. Otherwise, India will most likely continue to install inefficient coal plants, guzzle foreign oil and struggle with rickety grids. Rather than hoping that India builds a low-carbon future, foreign leaders need to step up to help India make that choice. There is a strong financial incentive to do so: by accelerating India's energy transition, countries can open a lucrative export market for their clean energy industries. And there is a larger imperative: the fate of the planet hangs in the balance. SA

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NEUROSCIENCE

SCHIZOPHRENIA'S UNYIELDING MYSTERIES

GENE STUDIES WERE SUPPOSED TO REVEAL THE DISORDER'S ROOTS. THAT DIDN'T HAPPEN. NOW SCIENTISTS ARE BROADENING THE SEARCH

BY MICHAEL BALTER

GROOMING BY AKANE ANJAWI *Susan Price, Inc.*

Photographs by Ethan Hill

LAST YEAR, WHEN RESEARCHERS IN CAMBRIDGE, MASS., ANNOUNCED THAT THEY HAD FOUND A GENE STRONGLY LINKED TO A HIGHER RISK OF SCHIZOPHRENIA, THE NEWS MEDIA REACTED WITH OVER-ZEALOUS ENTHUSIASM. A "LANDMARK STUDY," DECLARED BOTH THE *NEW YORK TIMES* AND THE *WASHINGTON POST*. "GROUNDBREAKING," TRUMPETED CNN. EVEN THE *ECONOMIST* DROPPED ITS NORMAL RESERVE: "GENETICS THROWS OPEN A WINDOW ON A PERPLEXING DISORDER."

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The hype was somewhat understandable. Historically, schizophrenia research has left a trail of disappointment. The biological basis of the illness, one of the most puzzling and complex mental disorders, has long been an enigma. The toll, however, has always been clear. In the U.S. alone, estimates place the total cost of caring for patients at more than $60 billion a year, a figure that includes both direct health care costs and indirect economic losses from unemployment and early death. Any breakthrough in understanding the causes of the illness would be a major medical advance.

Since the advent of large-scale genetic studies just more than a decade ago, hopes have risen that new insights and therapies were on the way. They are much needed. Existing antipsychotic drugs dampen only the most overt symptoms, such as delusions and hallucinations. They often cause serious side effects and do little or nothing for chronic symptoms such as social withdrawal and cognitive deficits.

But genetic studies have yet to deliver on this promise. Gargantuan gene studies for schizophrenia, as well as depression and obsessive-compulsive and bipolar disorders, have driven home the message that most likely no single gene will lead to new treatments. The study behind last year's exuberant headlines was no exception. If nothing else, though, that research provides an inside look at the immense difficulties in understanding the mental processes that veer off course in schizophrenia.

THE 1 PERCENT

SCIENTISTS WHO STUDY psychiatric disorders had solid reasons to think that genetic clues might help overcome the field's stagnation. Decades of family and twin research suggest a strong genetic component to schizophrenia risk—one underlined by the steady rate at which the disorder occurs. Its prevalence is estimated to be about 1 percent throughout the world, notwithstanding vast environmental and socioeconomic differences across societies. Geneticists also knew that the hunt would not be straightforward. Individual genes powerful enough to generate a high risk of schizophrenia were likely to be very rare in the overall population and thus relevant to only a small percentage of schizophrenia cases. More common genes, on the other hand, would have much smaller effects in triggering schizophrenia and thus be much harder to detect. To find them would require greater statistical power, which would mean working with big sample sizes—tens of thousands of cases and control subjects. Acknowledging the challenges at hand, scientists in 2007 launched the Psychiatric Genomics Consortium (PGC) to study schizophrenia and other mental disorders. At present, the PGC has more than 800 collaborators from 38 countries and samples from more than 900,000 subjects.

Michael O'Donovan, a psychiatric geneticist at Cardiff University in Wales and chair of the PGC's schizophrenia working group, says a global approach was essential to assembling the "truly enormous sample sizes" needed to do the job in what is known as a genome-wide association study (GWAS). A big splash came in July 2014, when the group reported a GWAS involving about 37,000 schizophrenia cases and 113,000 control subjects. The study identified 108 genes (genetic regions) linked to schizophrenia, including a number that code for brain-signaling systems, the main targets for current antipsychotic drugs. These correlations were a sign that researchers might be on the right track.

The genetic region that showed the strongest link to schizophrenia codes for proteins of the major histocompatibility com-

IN BRIEF

Massive genetic studies, it was hoped, would help discover the underlying causes of schizophrenia, a pyschiatric disorder that produces a toll in the U.S. of $60 billion annually for patient care. Research toward achieving this goal began about 10 years ago.

The findings have not lived up to their original expectations. Studies have made clear that no single gene will lead to new treatments and that the tangled genetic landscape of schizophrenia is at best a series of faint hints of what causes the illness.

The way forward will require that the field act on a mix of clues that suggest that early-life influences—such as childhood trauma and prenatal factors—exacerbate the impact of genes in elevating the risk of a diagnosis.

plex (MHC), which is intimately involved in recognizing molecules alien to the body and alerting the immune system. That discovery led Steven McCarroll, a geneticist at the Broad Institute of Harvard University and the Massachusetts Institute of Technology, to think that the MHC region might be a good target for additional study. When McCarroll's team probed further, it turned up a variant of *C4,* an MHC gene, that elevated schizophrenia risk from about 1 to 1.27 percent in the populations studied.

Although that is a relatively small increase, the researchers suggested in their report in *Nature* that it could hint at how some cases of schizophrenia arise. The *C4* results were important for other reasons as well. Variations in human *C4* consist not only of differences in the gene's DNA sequence but also of disparities in its length and how many copies of that gene an individual has.

From previous studies, scientists suspected that relatively rare copy number variations (CNVs) played important roles in schizophrenia—and they continue to debate whether key schizophrenia genes are likely to be uncommon variants that raise risk dramatically or common versions that increase risk only slightly. The new study provided strong confirmation of CNVs' tie to schizophrenia. And when the team compared the brains of both living and deceased schizophrenia patients with those of control subjects, it found that markedly more of the C4 protein was produced in the patients' brains, which was associated with the presence of additional copies of the gene.

To look more closely at what *C4* does at the molecular level, the researchers turned to mouse brains. Beth Stevens of the Broad Institute, who spearheaded this part of the study, found that the protein assisted in brain development by "pruning" neural connections, called synapses, when they are no longer needed. Synaptic pruning is a normal part of brain maturation. But if this process is overactive and pares back too many synapses, it could perhaps elucidate some of the features of schizophrenia. It might explain why affected patients tend to have thinner cerebral cortexes and fewer synapses. And schizophrenia, along with other forms of psychosis, is usually first diagnosed in people in their late teens or early adulthood, when brain maturation reaches its final stages.

For some scientists, the finding was a vindication for GWAS as a relatively new way to hunt down disease-associated genes. GWAS has triggered an "amazingly positive and unprecedented explosion of new knowledge" about mental disorders, says Patrick Sullivan, a psychiatric geneticist at the University of North Carolina at Chapel Hill School of Medicine. As for the *C4* study, David Goldstein, director of Columbia University's Institute for Genomic Medicine—who has long been a skeptic of GWAS's potential—says that by pointing the way to a possible biological pathway for schizophrenia, the new finding represents "the first time we have gotten what we wanted out of a GWAS." Others, including some leading geneticists, are less certain, however. "GWAS will have no impact on resolving the biology of schizophrenia," says Mary-Claire King of the University of Washington, who in 1990 identified *BRCA1* as a major risk gene for breast cancer.

In scientific parlance, most cases of schizophrenia appear to be highly "polygenic"—hundreds or perhaps thousands of genes are involved. "GWAS shows that schizophrenia is so highly, radically polygenic that there may well be nothing to find, just a general unspecifiable genetic background," says Eric Turkheimer, a behavioral geneticist at the University of Virginia.

Indeed, it might be argued that one of GWAS's most important contributions—and the *C4* study was no exception—has been to disabuse researchers of simplistic notions about psychiatric genetics. The new findings so far have dashed hopes that schizophrenia can be pinned on just one or even a few genetic mutations. The skepticism stems from the realization that each of the 108 genetic locations linked to schizophrenia so far confers only a tiny risk for the disorder. And the few genes that confer a high risk—in the case of copy number variants and other rare mutations—account for only a small percentage of schizophrenia cases. That makes it less likely that the new findings will lead to therapies anytime soon. It also poses obstacles for neuroscientists and psychiatrists who hoped to find genetic clues for the underlying roots of the disorder. "It would have been way better if there were one single gene," says Kenneth Kendler, a psychiatric researcher at the Virginia Commonwealth University's School of Medicine. "Then all of our research could have gone into that area."

In the case of *C4,* a recognition of these limitations has led to questions about just how relevant the gene will be to understanding schizophrenia or developing new therapies. Whereas about 27 percent of the nearly 29,000 schizophrenia patients in the study had the highest-risk *C4* variant, roughly 22 percent of the 36,000 healthy control subjects also carry it, according to McCarroll. "Even if the *C4* story is right, it accounts for only a trivial amount of schizophrenia," says Kenneth Weiss, an evolutionary geneticist at Pennsylvania State University. "How useful that will be is debatable." And the study does not prove a direct relation between synaptic pruning and schizophrenia, McCarroll and others concede. Its importance seems to lie more in its potential to help pinpoint what kinds of biological pathways might be involved.

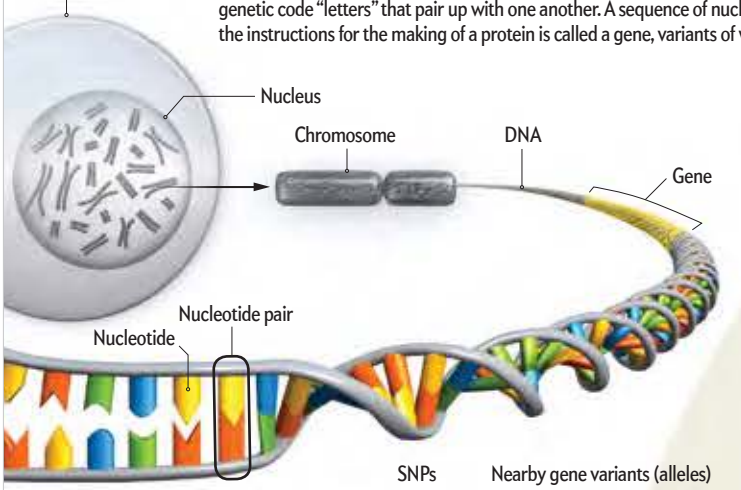
Still other problems beset GWAS. To procure huge samples, geneticists usually distinguish between cases and controls depending on whether a person has received a formal schizophre-

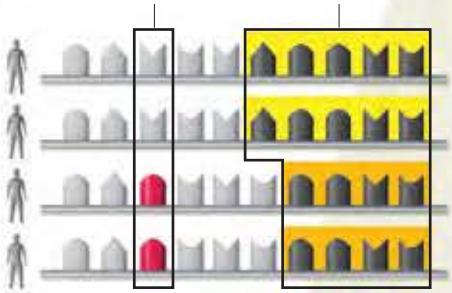
Research Dragnet Falls Short

When the first rough draft of the Human Genome Project appeared in 2000, the research community thought it might herald an era of personalized medicine that would bring new therapies for a range of diseases, including psychiatric illnesses, such as schizophrenia. Large-scale studies that have identified variations in the makeup of genes that elevate the risk of schizophrenia have not yet provided solid leads for new treatments.

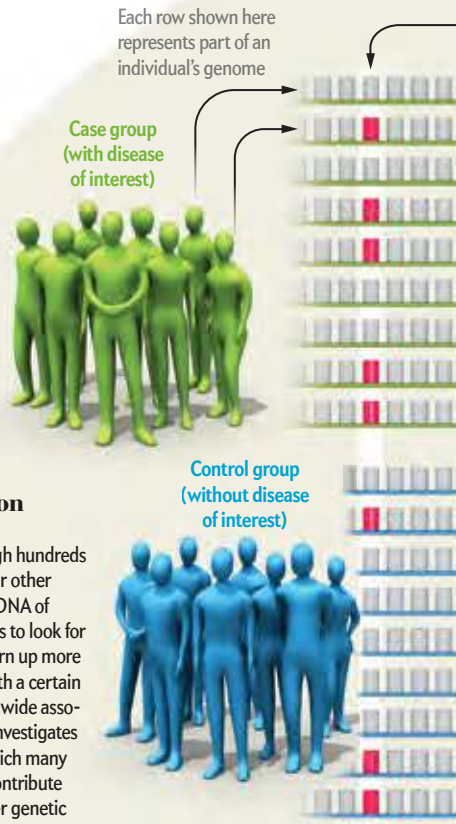
Basics

The nucleus—the cell's command center—houses 23 chromosomes, which consist of long, threadlike stretches of DNA. Building blocks of DNA, known as nucleotides, carry varying genetic code "letters" that pair up with one another. A sequence of nucleotides that provides the instructions for the making of a protein is called a gene, variants of which are called alleles.





SNPs: Certain variants (*pink*) in a sequence of DNA—single-nucleotide polymorphisms, or SNPs—contribute to disease risk or serve as signposts that indicate the presence of nearby alleles associated with an illness.



How Genome-Wide Association Studies Work

Researchers mill through hundreds or thousands of SNPS or other genetic variants in the DNA of thousands of individuals to look for genetic variants that turn up more frequently in people with a certain illness. Such a genome-wide association study (GWAS) investigates complex diseases in which many genetic variants may contribute to a person's risk. (Other genetic conditions may be caused by a mutation in a single gene.)

nia diagnosis or not. But the criteria are very broad. In the U.S., the diagnostic rules are dictated by the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders,* whereas many psychiatrists in other countries rely on the World Health Organization's *International Classification of Diseases.* In the criteria set out in both volumes, patients can have markedly different symptoms, ranging from delusions to hallucinations to cognitive defects, and still be diagnosed with a case of schizophrenia.

Hannelore Ehrenreich, a neuroscientist at the Max Planck Institute of Experimental Medicine in Göttingen, Germany, describes schizophrenia as "an umbrella diagnosis" rather than a distinct disease: "We are focusing on people who are on the extreme end of human experience, who are part of a continuum and not a separate category." William Carpenter, a psychiatrist at the University of Maryland School of Medicine and editor in chief of the flagship journal *Schizophrenia Bulletin,* does not go that far, but he acknowledges that schizophrenia is a group of disorders or symptoms and not a distinct disease. "That makes it a weak target for gene discovery," he says.

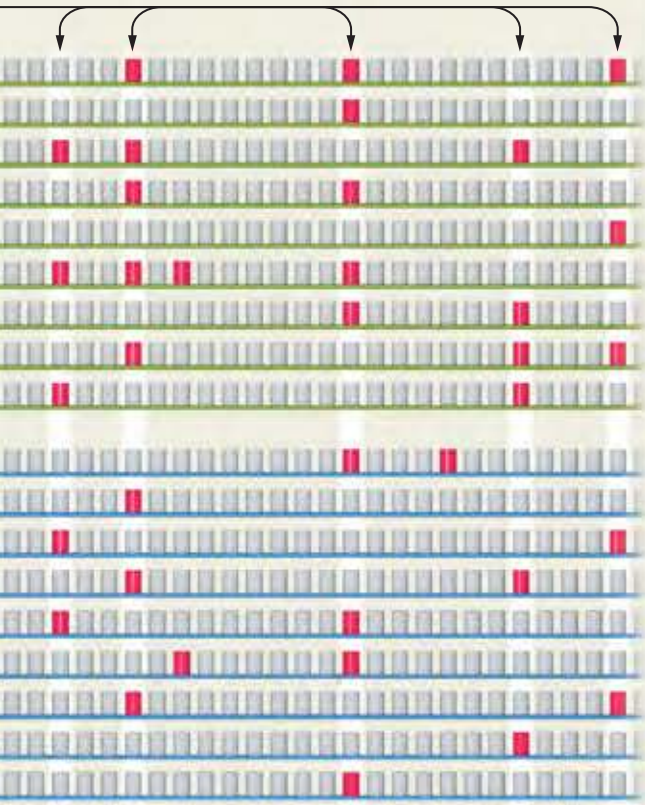
Goldstein, who thinks the *C4* findings "are the best case we've got" for understanding how a schizophrenia risk gene might exert its effects, still calls for researchers to express "a whole lot more humility" about GWAS results. "People working in the schizophrenia genetics field have greatly overinterpreted their results."

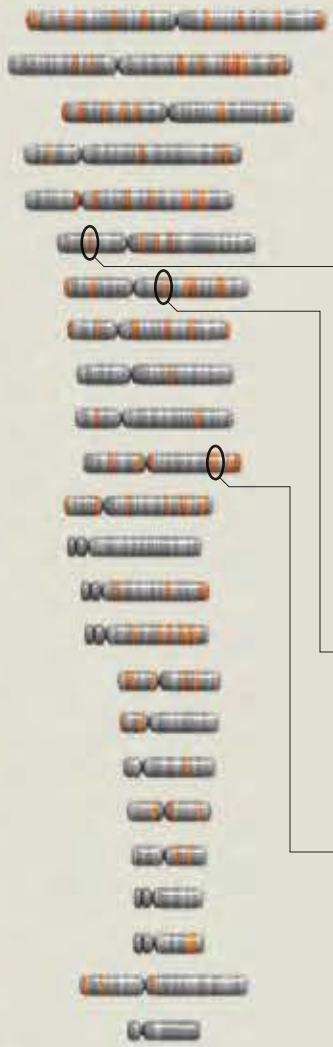
Some of the strongest skepticism about the search for schizophrenia genes comes from psychiatrists, patient advocates and former patients themselves. The GWAS approach focuses on finding new drugs to lessen symptoms of the disorder. But patients often look askance at this goal. "This obsession with symptom reduction does not entirely correspond with the viewpoint of the patients," says Jim van Os, a psychiatrist at the Maastricht University Medical Center in the Netherlands. Rather, van Os says, patients want to be able to live productive lives and function in society—and doing so does not necessarily correspond with being more medicated.

Graphic by Emily Cooper

GWAS scans the entire genome for differences between the disease and control groups. It employs sophisticated statistical analyses to pick up even small increases in the number of specific genetic variants that might contribute to disease risk.

SNPs more common in the disease group





Schizophrenia GWAS

A massive GWAS analysis published in 2014 identified 108 SNPs and other variants weakly correlated with schizophrenia from a study population of 37,000 schizophrenia cases and 113,000 controls. No single culprit emerged. But some of the variants helped to code proteins related to brain-signaling neurotransmitters; others were involved with the immune system. Here are three genes that stood out in this study and one in 2016.

C4: Helps with pruning synapses that are no longer needed. If this process is overactive, the immune-related protein may trim too many of these neural junctions, perhaps contributing to the dysfunction of schizophrenia.

GRM3: Involved with neural signaling by the neurotransmitter glutamate, the gene has several SNPs associated with schizophrenia. It has also been tied to other psychiatric disorders.

DRD2: Interacts with dopamine, a neurotransmitter implicated in schizophrenia. As a dopamine receptor, *DRD2* is the primary target of antipsychotic drugs.

SOURCE: "BIOLOGICAL INSIGHTS FROM 108 SCHIZOPHRENIA-ASSOCIATED GENETIC LOCI," BY SCHIZOPHRENIA WORKING GROUP OF THE PSYCHIATRIC GENOMICS CONSORTIUM, IN *NATURE*, VOL. 511; JULY 24, 2014 (*108 SNP details*)

Van Os and a growing number of patient advocates argue that the term "schizophrenia" itself is part of the problem because it stigmatizes and dehumanizes patients without adequately describing what is wrong with them. Jim Geekie, a clinical psychologist who works at a National Health Service inpatient unit just outside London, says that "knowing somebody's diagnosis tells me next to nothing about them."

Indeed, a number of countries and regions in Asia, including Japan, South Korea, Hong Kong and Singapore, have eliminated the classification altogether. The Japanese term "mind-split disease," used to describe a person with schizophrenia, has been changed to "integration disorder," and a similar term in Korean has been changed to "attunement disorder."

For many researchers and advocates, the main problem with the nomenclature—and with the gene search itself—is the lingering implication that patients are suffering from a form of brain disease. "If there are genetic variations that mean some people are prone to having these experiences, then we need to make sure people's environments don't switch these things on," says Jacqui Dillon, chair of the U.K.'s Hearing Voices Network. Dillon, who was told as a young woman that she had schizophrenia and still hears voices today, adds that understanding schizophrenia genetics "doesn't change what we need to do to keep people from going mad."

A DEEP FLAW

SOME RESEARCHERS INSIST that the search for genes is misguided because it largely ignores the environmental context, as well as the personal and family circumstances, that contributes to schizophrenia risk. "The whole enterprise is deeply flawed," says University of Liverpool psychologist Richard Bentall. This view is especially strong among clinicians, such as Bentall, who directly treat schizophrenia patients. They argue for increased funding for pragmatic, nonbiological approaches, ranging from family therapy to cognitive-behavioral therapy (CBT).

At times, questions also arise about the fundamental idea,

derived largely from family and twin studies, that schizophrenia has a high "heritability." This term is often assumed, even by many scientists, to mean that genetic factors play a major role. Yet the concept of heritability is complex and not a direct measure of how "genetic" a particular trait—such as a formal schizophrenia diagnosis—actually is [*see box at right*].

In fact, environmental and social factors, some researchers insist, confer a greater schizophrenia risk than most genes identified so far. Epidemiological studies have shown that risk factors range from living in an urban environment or being an immigrant to experiencing poverty and emotional and sexual abuse.

Just how such factors contribute to schizophrenia risk is not well understood, aside from speculations that they are sources of emotional stress. Recently, for example, an Israeli team found that Holocaust survivors suffered higher rates of schizophrenia. Another group found increased risk among people who had lived through the violent "Troubles" in Northern Ireland.

There is growing evidence that progress can be made only if researchers consider a spectrum of risk factors. Whereas genetics may make some people more vulnerable to mental disorders, influences from family or a social circle may push a susceptible individual across a threshold that results in a first psychotic episode. The key task is to figure out how genetic and environmental factors interact to produce schizophrenia.

Even diehard gene jockeys admit that environmental influences must be playing some kind of role. "Genes are not destiny," McCarroll agrees. He points out that when one member of a pair of identical twins is diagnosed with schizophrenia, the other twin is affected by the disorder only about half of the time—a clear indication that nongenetic factors must be important.

STATISTICAL MEASURES

Heritability: Missing or Just Hiding?

A concept that seems obvious is not

Researchers have been looking for schizophrenia-related genes for at least 50 years. What makes them think they will find them? The rationale is spelled out in the introduction to nearly every scientific paper on schizophrenia genetics: The disorder has a high heritability. This term is often interpreted as a measure of the relative role played by genes. Heritability is usually expressed as a percentage between 0 and 100 percent.

Scientists have estimated the heritability of schizophrenia using several approaches, including studies of twins. Most estimates hover around 80 percent. Many researchers argue that heritability estimates for schizophrenia can be very misleading, however. They question key suppositions, including the so-called equal environment assumption (EEA), which considers both identical and fraternal twins to be subject to the same environmental influences.

"These basic assumptions are wrong," says Roar Fosse, a neuroscientist at the Vestre Viken Hospital Trust in Norway, who led a recent critical assessment of the EEA. But twin researchers have mounted a vigorous defense of the approach. "I don't think it's likely that current heritability numbers are substantially overestimated," says Kenneth Kendler, a psychiatrist at the Virginia Commonwealth University's School of Medicine.

Some researchers have an even more profound critique of heritability. They argue that the technical calculations of the term do not account for the relative role of genes and environment. Heritability, rather, measures only how much the variation of a trait in a particular population—whether height, IQ or being diagnosed with schizophrenia—reflects genetic differences in that group.

As an example of how misleading heritability estimates can be, Eric Turkheimer, a geneticist at the University of Virginia, points to the human trait of having two arms. Nearly everyone in a given population has two of them, and there is normally no difference in the number of arms between identical twins—who share nearly 100 percent of their DNA sequence—and fraternal twins, who are assumed to share 50 percent of their genes on average. Thus, when heritability for arm number is calculated using standard heritability equations, it comes out to 0. And yet we know that having two arms is almost entirely genetically determined.

Figuring out what heritability for schizophrenia actually means is key, researchers say, because even the most high-powered genetic studies have identified only about a third of the predicted genetic component. Will this so-called missing heritability eventually show up in more sophisticated studies—or will it turn out that genes are not playing as big a role as heritability estimates have long predicted? The jury is still out. —*M.B.*

ENVIRONMENTAL ROOTS

FRUSTRATIONS IN THE HUNT for schizophrenia genes have forced the field to reassess how to move forward. Genetics is still considered important to understanding the biological underpinnings of the disorder and coming up with new drugs. But most researchers and clinicians now agree that a broader strategy that supplements genomic approaches is needed, one that builds on expertise gained from experts in sociology, psychotherapy and even prenatal health.

Over the past several years psychologists, psychiatrists, epidemiologists and social workers have accumulated a deeper understanding of the environmental and social factors underlying the disorder. Many new studies are now focusing on "childhood adversity," an umbrella term that includes sexual, physical and emotional abuse, neglect, bullying, and the loss of one or more parents.

One of the most widely cited of these studies, a meta-analysis by van Os and his colleagues, published in 2012 in *Schizophrenia Bulletin,* combined results from several studies to increase statistical power and found that patients suffering psychotic symptoms were nearly three times as likely to have been the victims of adversity, far greater than the risk of any gene identified so far in a GWAS. "We need a stronger focus on changing the environment so we can prevent schizophrenia," says Roar Fosse, a neuroscientist at the Vestre Viken Hospital Trust in Norway. "We

need to give children better childhoods and better chances to avoid extreme stress."

And in a 2014 paper in the *Lancet,* Ehrenreich and her colleagues demonstrated how studies that combine genetic and environmental data can provide new insights. The team reported on 750 male schizophrenia patients in Germany for whom—unusually—both GWAS and detailed environmental and social risk data were available. The team looked at the age of schizophrenia onset in these patients, a key indicator of how well they are likely to do over the long run: the earlier the age of onset, the worse the eventual outcome. It found that environmental factors, including early brain damage, childhood trauma, living in an urban environment, coming from an immigrant family, and especially cannabis use, were significantly associated with earlier onset. The average age of onset was nearly 10 years earlier for patients who had four or more environmental risk factors than for those who had none. On the other hand, so-called polygenic risk scores calculated from the GWAS data had no detectable effect on age of onset.

THE BIG QUESTION IS WHETHER THE SEARCH FOR GENES WILL EVENTUALLY LEAD TO NEW THERAPIES FOR SCHIZOPHRENIA. MOST SCIENTISTS AGREE THAT IT WILL TAKE MANY MORE YEARS FOR RESEARCH TO PAY OFF IN NEW DRUGS OR OTHER INTERVENTIONS.

Ehrenreich does not interpret these results to mean that genes are irrelevant. It is more likely, she says, that "the genetic factors are so different from one individual to the next that each person has a different reason for having the disorder." Other researchers, meanwhile, are looking at how environmental stresses, at home or school or through exposure to certain chemicals, might turn genes off and on—a pursuit known as epigenetics.

Ehrenreich and others urge GWAS researchers to begin incorporating environmental data into their studies whenever possible so they can derive a statistical model of how genes and environment interact to make people sick. "It is a shame that researchers neglect assessing environmental information in some of the most expensive and technologically advanced genetic studies," says Rudolf Uher, a psychiatric researcher at Dalhousie University in Nova Scotia.

Unfortunately, combining epidemiology with genetics may be a tall order. "The cost of gathering environmental data is enormous, and there is considerable disagreement about how to define these environmental variables," Cardiff's O'Donovan comments. Even so, in 2010 the European Union funded a five-year pilot program to do just that, led by O'Donovan, van Os and others—and researchers have now begun analyzing the data generated.

The big question, of course, is whether the search for genes, even in the context of environmental influences, will eventually lead to new therapies. Most scientists agree that it will take many more years for this research to pay off in new drugs or other interventions. Genetics "has provided the first hard biological leads in understanding schizophrenia," says Peter Visscher, a geneticist at the University of Queensland in Brisbane, Australia. "It is too early to say whether these discoveries will lead to new therapies, but there is no reason why they could not." Psychiatric researcher John McGrath, also at Queensland, agrees: "The science is hard, and the brain is hard to understand. But there is no need to throw our hands up in despair."

Meanwhile, in parallel with the genetic studies, schizophrenia researchers are pursuing numerous other lines of inquiry. They have begun looking for biomarkers—telltale molecules in blood or brain anomalies from neuroimaging that might help them identify people at high risk for the disorder. This could lead to earlier treatment, which numerous studies demonstrate can lead to a better long-term prognosis. Prompted by studies suggesting that the children of women who come down with infectious diseases during pregnancy might be at higher risk for schizophrenia—possibly because of immune responses harmful to the brain of the fetus—other teams are testing anti-inflammatory compounds to see if they might reduce symptoms.

A number of recent clinical trials, meanwhile, suggest that psychosocial therapies, especially CBT, can help lessen both symptoms and suffering in schizophrenia patients. While this research is controversial and the effects are only modest so far, advocates of such approaches are gaining traction in both Europe and the U.S. In the U.K., for example, CBT is now recommended by government health authorities for all first-episode cases of psychosis. "The imbalance in funding between genetic and pharmacological research and psychosocial research needs to be addressed and corrected," says Brian Koehler, a neuroscientist at New York University who also treats schizophrenia patients in private practice.

The intricacies of schizophrenia mean that comprehensive new treatments are still speculative. Researchers hope that one day brain imaging or other diagnostic tests may help spot a youngster at risk either before or during adolescence. If so, new medications and psychological counseling may be able to delay or prevent a first psychotic break. To achieve that goal, biologists and social scientists must continue to merge their expertise to piece together a composite profile of one of the most complex of all psychiatric illnesses. SA

MORE TO EXPLORE

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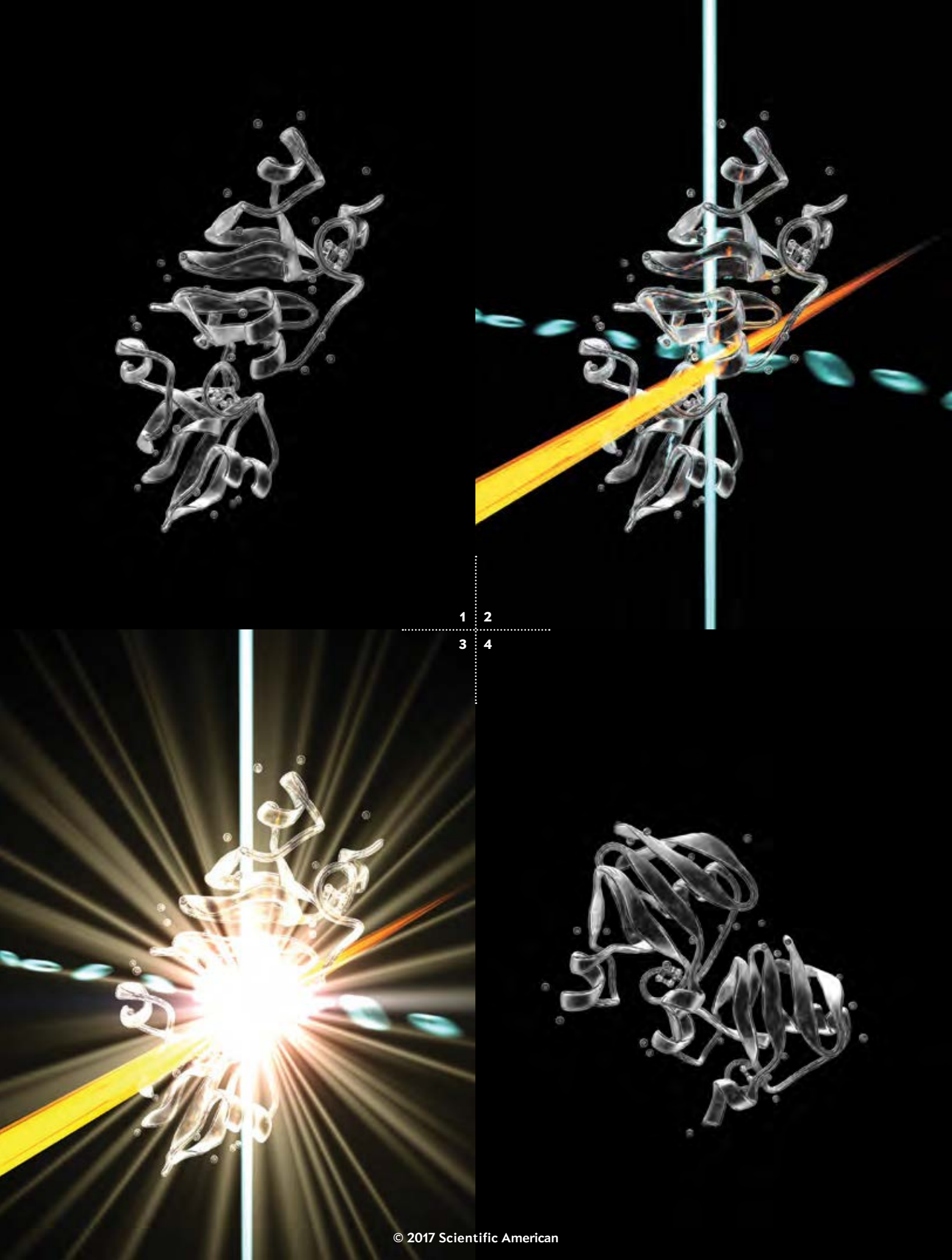


CHEMISTRY

SPLIT-SECOND REACTIONS

New movies of drug proteins or photosynthesis in action, shot in millionths of a billionth of a second, show how the molecules work—or fail

By Petra Fromme and John C. H. Spence

IN BRIEF

Proteins are in constant motion, carrying out the reactions that make life possible. These movements happen on a scale too small, and too fast, to be seen with microscopes.

Using x-ray laser pulses lasting just millionths of a billionth of a second, researchers have created "molecular movies" that show how proteins change structure when they interact.

These movies can reveal biological reactions in unprecedented detail and demonstrate why drugs sometimes do not hit target proteins and how plant photosynthesis creates clean energy.

Illustration by Bryan Christie

Petra Fromme is Paul V. Galvin Professor and director of the Center for Applied Structural Discovery at Arizona State University.

John C. H. Spence is Richard Snell Professor of Physics at Arizona State and director of science at the BioXFEL Science and Technology Center.

BURROWED DEEP UNDER THE FOOTHILLS NEAR PALO ALTO, CALIF., SCIENTISTS SCURRIED THROUGH AN UNDERGROUND LABORATORY, making final preparations for a series of explosions. ***THEIR PLAN:*** blow up tiny crystals of proteins that could reveal one of nature's best-kept secrets—how plant photosynthesis turns light into chemical energy. The potential payoff: a step toward unlimited clean power.

It was December 2009, and a sleep-deprived team of researchers and students at SLAC National Accelerator Laboratory had been working nonstop for days to set up this experiment at the world's most powerful x-ray laser, the Linac Coherent Light Source (LCLS), which accelerates electrons to nearly the speed of light. One group feverishly adjusted injectors that would shoot crystals of proteins into the x-ray beam. Another locked and loaded the injector with fresh crystals of a protein complex called photosystem I, which is key to photosynthesis.

At the end of the two-mile accelerator tunnel, the crystals began their march into the intense laser light. But before each of them exploded, its snapshot was taken with a newly developed scientific technique. Today that method promises to reshape our understanding of biology on the tiniest scale because we can now assemble a rapid sequence of such images—shot in femtoseconds, or millionths of a billionth of a second—into movies.

Physicist Richard Feynman once said, "Everything that living things do can be understood in terms of the jigglings and wigglings of atoms." But never before have we been able to directly see the wiggling of atoms and molecules within living things at this speed. Our method, called serial femtosecond crystallography (SFX), lets us watch high-speed molecular dances that determine how medicines affect diseased cells and how chemical reactions convert energy to different forms.

Already research teams around the world have used SFX to reveal fine details of how an experimental drug regulates blood pressure—paving the way to better hypertension medications. SFX has also shown the structure of the enzyme that destroys red blood cells in sleeping sickness, a fatal disease caused by parasites. And it has yielded the first look at the initial steps during photosynthesis that split water into hydrogen and oxygen.

Back in that underground lab in 2009, the stakes were high as x-ray pulses began to annihilate our carefully formed crystals. Many scientists had said SFX would never work and rejected our requests for funding. But then beautiful images of scattered x-rays began to emerge on computer screens. We still remember our cheers erupting around the room as we watched what would become proof that a new field of x-ray science had been born.

X-RAY VISION

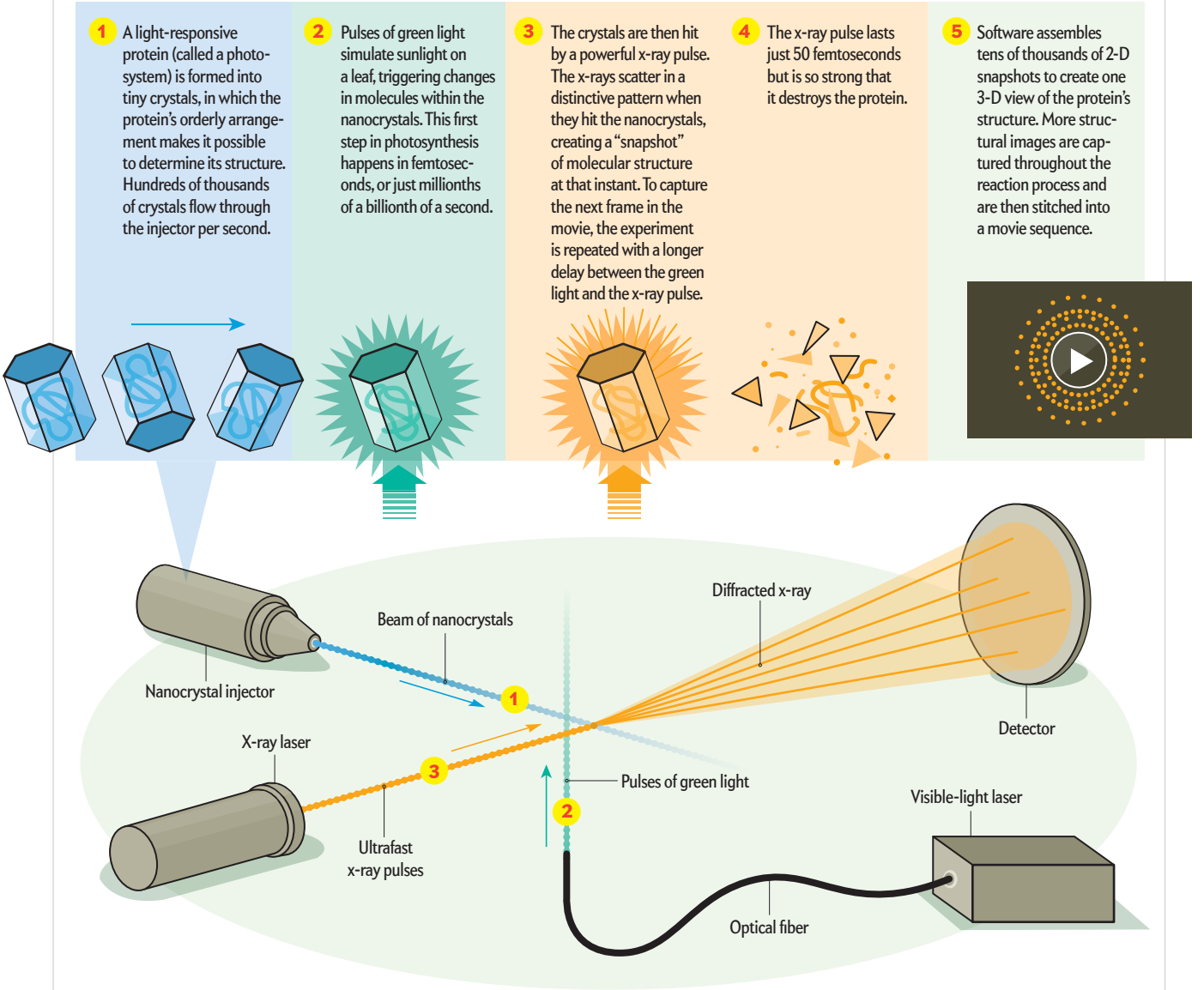
BEFORE SFX, scientists made amazing advances in detecting the changes of certain chemical structures, but they could not actually observe the most delicate and complex biological structures in action. In the 1980s, for instance, the late chemist Ahmed H. Zewail invented a way to watch atoms move during chemical reactions using ultrafast pulses of visible laser light. Yet the light's wavelength was too long to distinguish the tiniest details of protein structure. More recently, dramatic advances in microscope technology have produced near-atomic-resolution images of proteins and viruses. But they are not quick enough to capture rapid reactions such as photosynthesis.

We decided to use x-rays, which have the necessary speed and resolution to record biological reactions in action. Key to our work was developing a technology that would allow x-rays to form pictures of molecules in the instant before destroying them. Traditionally scientists who do this work painstakingly grow large crystals of proteins and other molecules to map the positions of atoms within them. Then they bounce x-rays off the crystals and record the pattern of x-ray scattering, or diffraction. In a crystal, molecules are held in place in an orderly arrangement, so the x-rays scatter in predictable ways, allowing scientists to interpret the position and identity of atoms. This method is called x-ray crystallography, and our serial femtosecond crystallography uses the same principle to see atomic structure but does so far faster.

X-rays ultimately destroy the molecules we are trying to see, however. It was commonly believed that the x-ray laser, which concentrates high-energy x-rays into a powerful beam, would

Moviemaking on a Molecular Scale

Photosynthesis makes life on earth possible by converting sunlight into chemical energy. A new kind of molecular movie has given scientists their first glimpse of the process in action. Researchers use visible light, simulating sunlight on a leaf, to spur proteins to begin photosynthesis, then use a powerful x-ray laser to take snapshots of changes in these proteins in the fractions of a second before they are destroyed. Snapshots are made in five steps (*shown below*) and combined into a movie.



only make matters worse. The laser's bright light alone can punch a hole through steel. A fragile biomolecule, one would think, would not stand a chance. We needed to outrun the x-rays' damage and capture an image in femtoseconds. For perspective, the difference between one femtosecond and one full second is equivalent to the difference between a second and 32 million years.

The key to the SFX technique lies in that imperceptible sliver of time between the molecule being struck by the x-ray laser pulse and electrons being ripped off its atoms by x-ray energy. Stripped of electrons, the positively charged remnants repel one another, causing the molecules to expand and ultimately explode.

Here is how it works: First, we prompt molecules to interact to form a tiny crystal. Then we shoot a powerful x-ray beam at the crystal in an extremely short pulse, just long enough for some of the x-rays to scatter off the crystal before the beam's energy rips the molecules apart. Finally, a detector captures the bounced x-rays, whose pattern reveals the type and position of

Illustration by Lucy Reading-Ikkanda

atoms in the protein. By capturing images of a stream of protein crystals as they tumble through the x-ray beam at different angles, we can re-create the structure in 3-D. Finally, we can collect images at different time points in a reaction and put the pictures together in sequence, like images in a film strip.

CRYSTALLIZED VIEW

THE FIRST STEP toward making these molecular movies came in 2000, when biophysicists Janos Hajdu and Richard Neutze, both then at Uppsala University in Sweden, calculated that it would take roughly 10 femtoseconds for molecules to begin exploding after being hit by x-rays. Thus, scientists needed to take a snapshot faster than that. In 2006 Henry Chapman, now at the German Electron Synchrotron (DESY), and his colleagues were able to do just that using a "diffract then destroy" approach to capture a low-resolution image of two tiny stick figures and the sun etched into a silicon nitride membrane.

But would this work for delicate biological molecules? Much of the scientific community was skeptical when we proposed to try. Our first 10 grant proposals were all rejected. Doubters said that the x-ray laser pulses would not be short enough, or the protein crystals would be too small to give any detectable signal, or we would never be able to figure out the crystal's orientation when it was struck by the x-ray pulse, information needed to determine its structure.

SPOT ON: With serial femtosecond crystallography, the gray dots in these panels show patterns of x-rays after they collide with protein crystals, revealing their structure.

But we thought that if other kinds of molecules could be imaged, as Chapman had proved, then biomolecules could be, too. One of us (Fromme) and her team sought to prove SFX using one of the most difficult tests imaginable: photosystem I. Consisting of 36 proteins and more than 300 light-capturing green and orange pigments, it is among the most complex protein structures analyzed with x-rays to date.

Fromme knew photosystem I intimately, having worked for years to crystallize it and determine its structure using other methods. We also thought that the biomolecular complex's large size could actually be an advantage because with even a small number of diffraction patterns, we could get a low-resolution image that would be recognizable as photosystem I. And this is what we were able to do in that underground lab in 2009.

SMALL IS BEAUTIFUL

TO GET OUR SNAPSHOT, we first needed crystals of photosystem I. In typical crystallography, scientists grow large crystals, which have long been necessary to create enough x-ray scattering to reconstruct a protein's structure. But it can take years of experimentation to grow large, well-ordered crystals of some proteins. Several have proved nearly impossible, and photosystem I was one of them.

Instead SFX uses nanometer-sized crystals, which are much easier to grow in the lab. Using nanocrystals meant new challenges, however. Not only would we have to get a strong enough signal from such a small crystal, but we faced some basic physical challenges: How do you detect nanocrystals too small to see under a microscope, much less position them in front of x-ray pulses and do so consistently 120 times each second?

First, we had to invent new ways to see our nanocrystals. One of the methods we applied is called SONICC (second-order nonlinear imaging of chiral crystals), in which the crystals convert two ultrafast pulses of infrared light into one green photon—this lights up the nanocrystals like fireflies in the night so that we can detect them.

Another invention shoots the crystals into the x-ray laser pulse at a consistent clip. One of us (Spence), along with Arizona State physicists Uwe Weierstall and Bruce Doak, came up with a device that functions much like an inkjet printer, firing a stream of nanocrystal-containing solution across the x-ray beam. This injector fires nanocrystals so precisely that they march into the beam in a single-file line.

To keep the injector from clogging—which could shut down the stream of nanocrystals—Weierstall had to design a wide nozzle that still had the ability to produce a narrow stream. He did this by surrounding the outer end of the nozzle with a stream of helium gas, focusing the stream of crystals to a tiny fraction of a human hair even though the nozzle itself was more than 10 times larger.

Once we had all the machinery in order, we faced one more problem: how to master a Mount Everest of data. A single experiment can generate up to 100 terabytes of data, enough to fill 25 top-of-the-line desktop computer hard drives. And to construct a 3-D view, we have to find, then merge, the correct orientation of each of the crystals in tens of thousands of snapshots. So we developed special software in collaboration with Richard Kirian and Thomas White, both then members of Chapman's team at DESY. With the new software, we can turn our tsunami of data into accurate 3-D images of a molecule.

Step by step, we improved our technique. And by 2014 our work gave us the first real-time glimpse of the transfer of electrons between two key players in photosynthesis: the large sunlight-catcher photosystem I and a protein called ferredoxin.

When light hits photosystem I, it is converted into electrons, which ferredoxin then carries away to be used for converting CO_2 into biological molecules. When ferredoxin leaves, the protein crystals quickly dissolve, making the reaction difficult to follow. Only the superfast process of SFX can see the rapid change.

The next challenge in this line of research is a big focus of Fromme's work as a biochemist: unraveling how a plant splits water into hydrogen and oxygen using just sunlight and the earth's abundant metals. Splitting water the way that a plant does could provide cheap, clean-burning hydrogen as fuel for cars and power generators, a long-held dream for developing a renewable energy economy.

FROM "SERIAL FEMTOSECOND CRYSTALLOGRAPHY DATASETS FROM G PROTEIN-COUPLED RECEPTORS." BY THOMAS A. WHITE ET AL., IN *SCIENTIFIC DATA*, VOL. 3, ARTICLE NO. 160057. PUBLISHED ONLINE AUGUST 1, 2016

SCIENTIFIC AMERICAN ONLINE See how a molecule responds to light at the atomic level at ScientificAmerican.com/may2017/molecular-movie

WITH SFX, THE FILMS WE PRODUCE COULD LEAD NOT ONLY TO FUTURE BREAKTHROUGHS BUT MORE IMMEDIATELY TO NEW AND BETTER MEDICATIONS.

We have gathered the first low-resolution snapshots of the water-splitting process and see an initial hint of significant structural changes to the protein complex involved, photosystem II. Just recently Jian-Ren Shen's group at Okayama University in Japan has applied the SFX technique to show the same snapshot of the process at even more detail. Next, we seek to make high-resolution movies showing details of all stages of the process at the atomic level and to discover the secret of photosynthesis.

DESIGNER DRUGS

NOW THAT SCIENTISTS have begun making movies using SFX, the films we produce could lead not only to future breakthroughs but also more immediately to new and better medications. We saw this potential when we studied angiotensin II receptor blockers (ARBs). These drugs interfere with a cell receptor for the hormone angiotensin II, which constricts blood vessels. ARBs are used to treat high blood pressure (hypertension), the leading cause of stroke and heart failure in the U.S. Whereas the first generation of these drugs has proved useful, the drugs bind to their targets only weakly and must be used in high doses, worsening their side effects, which can include headaches and dizziness and occasionally more serious problems such as swelling in the face and throat.

Our research has revealed the reason behind the poor binding: the drugs really do not fit the receptor as well as they should, so many of their molecules fall away. More accurate structures of the receptors could lead to new ARBs that will more effectively control blood pressure. And in fact, one drug called ZD7155 is already being evaluated.

These refinements could improve many other drugs, too. Angiotensin II receptors belong to a larger and extremely important group of cell receptors called G-protein-coupled receptors. These cell-surface molecules allow a cell to sense and respond to its environment. The scientists who first uncovered the structure and actions of this receptor class won the 2012 Nobel Prize in Chemistry for the breakthrough. The vital role that G-protein-coupled receptors play in cell survival and growth makes them crucial targets for new drugs. Being able to see how their structures change will help pharmaceutical chemists design drugs that fit the receptors precisely and in their active state, thereby reducing the chance of side effects.

"We have shown that in all the previous molecular models, the best guesses for how receptor and drug fit together were wrong in many important details," says Vadim Cherezov of the University of Southern California, who conducted the angiotensin II experiment. For example, SFX has revealed differences in the structures of G-protein-coupled receptors at room temperature compared with the cryogenically cold temperatures traditionally used in crystallography—meaning that drugs designed for receptors at frozen temperatures will not fit properly when used in the warm human body. (Sometimes drugs hit too broad a target. This is the problem for drugs used to treat sleeping sickness. Our motion pictures have shown that the drugs interact in similar ways with proteins from the parasite that causes the disease and with proteins from human cells. Our more precise images give chemists a chance to make drugs that affect only the parasite protein, not people.)

EYES HAVE IT

WE HAVE ALSO BEEN THRILLED to see how other researchers are using our SFX techniques to answer different questions. Marius Schmidt of the University of Wisconsin–Milwaukee and his colleagues, for example, recently used molecular movies to help explain how our eyes can see. Although we do not typically think of bacteria as being capable of sight, they have light-responsive proteins that are the evolutionary precursors of those in our own visual system. By capturing snapshots faster than ever achieved before, the team made an ultraslow-motion video of extremely rapid events, revealing how a protein in bacteria senses and responds to light.

The group used SFX to capture images of the crystallized protein as it reacted to light in increments of less than a trillionth of a second. Specifically, the team mapped the protein's atoms in motion as a dye molecule buried within the protein turned yellow in response to light. For the first time, the structure of the yellow dye was captured immediately after it absorbed the light and before it could react; this state is fundamental to light perception in all living organisms, including bacteria and plants, and is the first event in human vision.

Seeing how this protein responds to light not only helps us understand how vision arose but also gives us an unprecedented look at how a biological reaction unfolds on chemistry's ultrafast timescale. "This puts us dramatically closer to understanding the chemistry necessary for all of life," Schmidt says.

We are convinced that the future of protein crystallography—as well as our knowledge of nature—lies with the SFX method. And who knows—perhaps within 10 years, half of all known protein structures will not be static images on a textbook page but 3-D movies. SA

MORE TO EXPLORE

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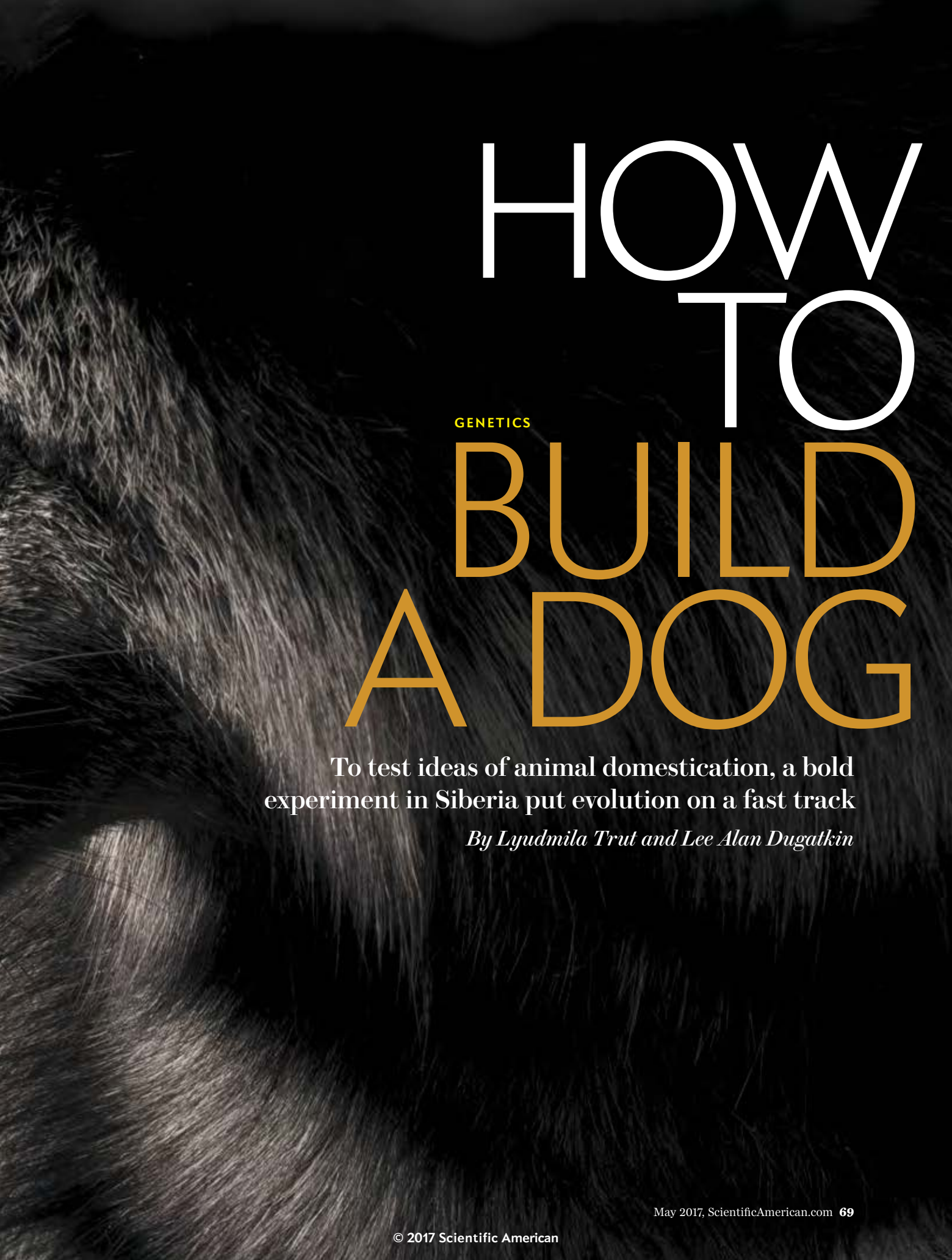
scientificamerican.com/magazine/sa

HUMAN LIFE SPAN was sufficient time to select for traits that have transformed foxes from wild to doglike.



GENETICS

HOW TO BUILD A DOG

To test ideas of animal domestication, a bold experiment in Siberia put evolution on a fast track

By Lyudmila Trut and Lee Alan Dugatkin

Lyudmila Trut is an evolutionary geneticist and a professor at the Institute of Cytology and Genetics in Novosibirsk, Russia, where the fox-domestication experiment takes place. She has lived this story, told in her voice, since 1959.

Lee Alan Dugatkin is a behavioral ecologist and a historian of science at the University of Louisville. For the past six years he has been collaborating with Trut on a book about the fox-domestication study.

The animal runs toward me, its curly tail wagging and its loving eyes full of joy. It jumps into my arms and nuzzles my face, like a dog. But it is not a dog. It is a fox—a fox that looks and behaves much like a dog. The animal and its close relatives are the result of 58 generations of selective breeding, performed in an attempt to discover in general the secrets of domestication and in particular how humans may have transformed wolves into the first dogs.

1

I am now 83 years old. As I look back on the experiment to which I have devoted three quarters of my life, my thoughts sometimes drift to Antoine de Saint-Exupéry's classic story *The Little Prince* and the fox's admonition to the prince that "you become responsible forever for what you have tamed."

I have thus been responsible for these foxes since shortly after I first met my mentor and friend Dmitri Belyaev in 1958. I was finishing my studies at Moscow State University when I heard that Belyaev was heading to Novosibirsk to join the new Institute of Cytology and Genetics and was looking for students to be part of a domestication experiment he was about to start.

In my first meeting with Belyaev, I was struck that he treated me, a mere undergraduate, as an equal. He explained the basic idea of the research, which was to study the process of domestication at fast-forward speed: "I want to make a dog out of a fox," he said. Generation after generation, we would selectively breed those foxes that interacted in the most positive ways with humans. If such a process worked as we thought it would, domestication—perhaps akin to the transformation that occurred to turn wolves into dogs—would unfold before our eyes.

By the time I left Belyaev's office, I wanted in—which meant moving to Novosibirsk, the major city in Siberia. I was excited by the prospect of becoming part of the first generation of researchers in Novosibirsk's new "scientific city" of Akademgorodok, which housed the fledgling institute, and by the prospect of working with a man I sensed was a revolutionary thinker. Soon my husband, baby daughter and I were heading east on the long train ride from Moscow.

Belyaev's hypothesis about the process of animal domestication was both radical and simple. He had come to think that the defining characteristic of all domesticated animals was their tameness. Therefore, from an evolutionary perspective, the pro-

PRECEDING PAGES AND THIS PAGE: VINCENT J. MUSI *National Geographic*

IN BRIEF

Wild wolves were transformed into domesticated dogs in only the past few tens of thousands of years. Humans clearly played a role in the speciation, but the details are lost to history.

A six-decade experiment in Siberia has attempted to replay the process by which wolves evolved into dogs. In this work, another canid species—wild foxes—were selected for tameness over dozens of generations.

Within a few generations, foxes emerged that behaved like pets and that had physical characteristics associated with domestication, including mottled coats and curly tails.

2

3

FOXES AND RESEARCHERS pose at their Siberian facility (*1* and *2*). Author Lyudmila Trut pets Pushinka's pup Penka in 1974, when all three shared a house (*3*).

VINCENT J. MUSI *National Geographic* (2); COURTESY OF LYUDMILA TRUT AND INSTITUTE OF CYTOLOGY AND GENETICS (3)

cess of domestication was primarily driven by our ancestors favoring animals that were the least aggressive and least fearful toward humans. Tameness was the key to working with animals to breed them for the other traits we wanted. Our dogs, cows, horses, goats, sheep, pigs and cats had to be docile, regardless of whether we were looking for protection, milk, meat, companionship, or other goods or qualities.

What is more, Belyaev thought that most, if not all, of the other characteristics that many domesticated animals possess, what we now call the domestication syndrome—curly tails, floppy ears, mottled fur pattern, the maintaining of juvenile facial characteristics (roundness and a blunted snout) into adulthood, and less reliance on strict seasonal breeding—were by-products of selecting for the tamest animals. And so, generation after generation, under Belyaev's guidance but also with a fair share of autonomy dealing with day-to-day experimental issues, I selectively bred the tamest foxes from animals that we initially collected from fox-fur farms around the Soviet Union.

MEET THE ELITES

EVERY YEAR I MADE INITIAL TESTS on hundreds of foxes, using a standard procedure that we developed. Wearing two-inch-thick gloves for protection, I approached each fox in its cage, stood by the closed cage, opened the cage door and placed a stick inside the cage. I scored the foxes' reactions on a scale that gave the calmest individuals the highest totals.

In the first years the vast majority of the foxes seemed less like dogs than like fire-breathing dragons: they were extremely aggressive when I approached or put the stick into the cage. I am sure these low scorers would have loved to rip my hand off. Other low-scoring foxes cowered in fear at the back of their cages. But a small number of animals remained calm throughout the test, observing but not reacting one way or the other. These animals were selected to mate and produce the next generation. I kept detailed records about every stage of development from newborn to adult. And we were especially careful to avoid inbreeding that would occur via the mating of close relatives—we hoped thus to avoid negative genetic consequences as a confounding factor in the experiment.

Even the calm foxes of the first few generations were not especially prosocial toward people—they seemed to tolerate, but not enjoy, the presence of humans. But I got a tantalizing hint of what was to come in the fourth and fifth generations: pups barely able to walk would wag their little tails in anticipation as I approached. Then came generation six.

As my colleagues and I wrote in 2009 in the journal *Bioessays,* "In the sixth generation, there appeared pups that eagerly sought contacts with humans, not only [tail] wagging [but] also whining, whimpering, and licking in a dog-like manner." The emergence of this constellation of behaviors was so striking we dubbed the animals the "elites." These little foxes even looked up when they heard their names. It appeared that they "yearned for human companionship," as we noted in our contribution to the second edition of a volume entitled *The Genetics of the Dog* in 2012. The tame pups also responded to sounds two days earlier and opened their eyes a day earlier than was typical for foxes, almost as if they were preparing to start interacting with people as soon as possible.

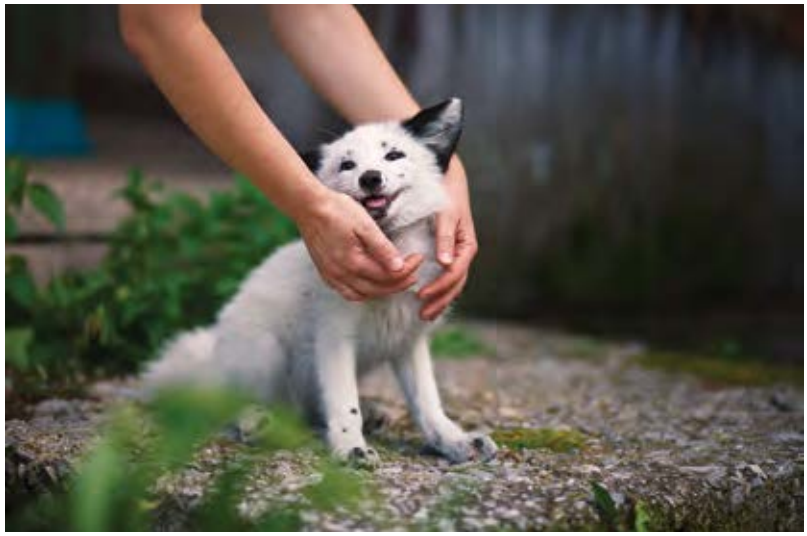
The elites charmed every human they met, no matter how toughened. One evening after the staff went home, Belyaev brought a famous army officer, a General Lukov, to our facility. Lukov was a formal man, hardened by the horrors of war. But when I opened a cage that housed one of the elite females and the fox scampered over and laid down next to me, the general's dignified demeanor melted away. Apparently astonished, he approached the fox, squatted down and petted its head at length.

In that sixth generation, the elites made up but 2 percent of our domesticated foxes, but that would increase with each generation. Today the figure sits at about 70 percent.

FETAL TRANSPLANTS

BELYAEV AND I WERE GENETICISTS by training, and any experiment on domestication is an investigation of evolutionary genetics. We needed to be certain that the changes we saw in the domesticated foxes were genetic in origin. Thus, we developed a test involving tame foxes as well as foxes from another experimental group we had developed—animals selected for their aggression toward humans. Generations of breeding had produced what we thought of as a fox equivalent of Cerberus, the multiheaded hound of Hades that guards the gates of the Underworld. These were mean foxes.

Our idea was to move embryos from tame mothers into the wombs of aggressive females, and vice versa. If the newborn pups behaved like their biological, rather than their surrogate mother, we could be confident that tameness and aggression were fundamentally genetic.



DOMESTICATED PUP enjoys human contact. Its rounded snout and mottled fur differ from those of its ancestors.

Every transplant involved a pair of females, one tame and one aggressive, each about a week into pregnancy. After anesthetizing the two females, I made a surgical incision into the abdomen of one and located the uterus, with its right and left "horn," each of which contained implanted embryos. I then removed the embryos from one horn of the donor female, gently placing them in a nutritive liquid. Then I repeated the surgical procedure, removing the embryos from one horn of the recipient female but this time replacing those with the embryos from the donor. In some of the transplants, the donor was a tame female and the recipient an aggressive female. In other transplants, the roles were reversed.

But when the pups were born seven weeks later, how would I know which litter members were the genetic offspring and which were the transplants? The foxes themselves came to the rescue here—coat color is a genetic trait in these animals, so by carefully recording the coat colors of their parents, the pups' coats would act as a marker of their lineage.

My longtime friend and colleague Tamara Kuzhutova and I recorded the pups' behavior as soon as they began interacting with humans. I particularly remember an aggressive female and her pups, only some of which were aggressive. Her foster tame offspring were barely walking, but if there was a human standing by they were already rushing to the cage doors and wagging their tails. This improper behavior appeared to vex the mother—she growled at the tame pups, grabbed their necks and threw them back in the nest.

In that same litter, the genetic offspring of the aggressive mom comported themselves in keeping with their mother's expectations: they growled aggressively and ran on their own to their nests. We saw this pattern repeatedly—pups behaved like their genetic mothers, not their surrogate mothers. Tameness and aggression toward humans thus appeared to be genetic traits.

PUSHINKA

BY 1974 WE WERE 15 GENERATIONS into the experiment. Many of the tame foxes fell into the elite category and were also showing an array of the characteristics seen in other domesticated species, as Belyaev had predicted. Their faces had become more juvenile in appearance, their tails were bushier, the levels of their stress hormones were lower and their reproductive cycles lasted longer. A few, including a favorite of mine named Mechta ("dream"), even had floppy ears.

Most domesticated species do not form close relationships with specific humans, but dogs are different. Might this emotional affinity for people be a change that could emerge quickly, as with so many other changes we had seen in the foxes? And would living with a human come naturally to the foxes we had domesticated? To seek answers, I proposed to Belyaev that we could use our genetically tame foxes to examine deep interspecies emotional bonds akin to those that form between humans and dogs.

The fox farm at which we ran the experiment included a small house. I proposed that I move into the house with one of the elite foxes to see what bonds might develop between us. Belyaev enthusiastically agreed. And so, on March 28, 1974, Pushinka, Russian for "tiny ball of fuzz," and I moved in together.

Pushinka had coal black eyes, silver-tipped black fur and a stripe of white on her left cheek. She had recently had her first birthday and was pregnant, just a week or two from delivering. I could therefore observe not only how Pushinka adjusted to living with me but also whether pups born in the company of humans might socialize differently than other pups, even elites, did.

Our new home had three rooms plus a kitchen and bathroom. I staked out one room to serve as bedroom and office, and I built a den in another room for Pushinka. The third room acted as a common area, with a couple of chairs and a table. Pushinka was free to roam anywhere in the house. So that I could also have some time with my human family, Kuzhutova and a few others helped out by taking over some days and nights. Whoever was on shift made detailed journal entries throughout the day and evening about all aspects of Pushinka's behavior.

COURTESY OF LYUDMILA TRUT AND INSTITUTE OF CYTOLOGY AND GENETICS

SCIENTIFIC AMERICAN ONLINE Hear Dugatkin on the fox-domestication study at ScientificAmerican.com/may2017/dugatkin

The first few days were a roller-coaster ride. When Pushinka moved in, she raced around the house, clearly agitated. She would not eat anything until I gave her a little piece of cheese and an apple that I had prepared for myself. On day two, things improved. When I returned after a short trip away from the house, Pushinka met me at the door—like a dog does. But Pushinka's mood swings continued. She could be so jittery that my new friend seemed at the edge of a nervous breakdown, but the next day she quietly jumped up on the bed and curled up beside me.

Although the adjustment had been rougher than I anticipated, after a week or so Pushinka settled down. She lay by my feet while I worked at my desk. She appeared to savor going out for walks with me. In one of her favorite games I would hide a treat in my pocket, and she would try to snatch it out. Sometimes she would lie on her back, inviting me to pet her exposed belly.

On April 6, Pushinka gave birth to six pups. And to my amazement, she carried one of her pups over to me and placed it at my feet. "Shame on you!" I remember saying, "Your pup's going to get cold!" But when I brought the pup back to the den, Pushinka again presented it to me. We went back and forth for a few rounds before I surrendered and did not bring the pup back to its nest.

I gave the pups names, all starting with P in Mom's honor: Prelest ("gorgeous"), Pesnya ("song"), Plaksa ("crybaby"), Palma ("palm tree"), Penka ("skin") and Pushok (the masculine version of tiny ball of fuzz). Within a couple of weeks the pups would come running out of their den when I entered the room.

Each had a distinctive personality: Pushok was an attention hog, Palma enjoyed jumping onto tables, Pesnya was stoic, Prelest sometimes bullied her siblings, Plaksa made mumbling sounds as she walked around, and Penka, my favorite, was a champion nap taker.

Despite Leo Tolstoy's claim that "all happy families are alike," Pushinka and her pups were a family both happy and unique. I would play ball with them all or run around to be chased by the little ones. Penka was especially fond of the latter activity, jumping on my back when she caught me. Especially rambunctious outings wore out the pups. One of my journal entries describes them as "sleeping, with no worries and with no fear."

As her offspring grew and she could spend less time watching over them, the bond between Pushinka and me deepened. She would lie by my feet and wait for me to scratch her neck. If I popped out of the house for a bit, Pushinka would sometimes sit at the window, looking out in anticipation of my return. And on seeing me approach the house, she would wait at the door, wagging her tail.

Despite all these signs of our connection, nothing could prepare me for the events of the evening of July 15, 1974. I was reading a book on the bench outside of the house, as I did often, while Pushinka rested at my feet. I heard footsteps in the distance but thought nothing of it. Pushinka, however, sensed danger. But rather than hiding or seeking my protection, she sprinted toward the perceived intruder and did something that I had never seen her do before or would see again: she barked, sounding exactly like a guard dog.

Never before had Pushinka acted in a truly aggressive, let alone fierce, manner to any human. I ran over to discover that it was just the night guard patrolling the facility who had spooked Pushinka. I began speaking to the guard in a calm voice. Pushinka, apparently sensing that all was well, stopped barking.

We had moved into the house three and a half months earlier to see whether living with a human would elicit a doglike loyalty in elite foxes that were the product of some 15 years of genetic selection. I consider that night to have provided the decisive answer.

DOWN TO THE DNA

PUSHINKA IS LONG GONE. But the experiment, and my involvement, continues to this day. Forty-three generations have followed Pushinka's. (Forty-three human generations ago would put us somewhere in the High Middle Ages.) The descendants of Pushinka and of her tame peers have provided insight after insight into the process of domestication, delineated in our book *How to Tame a Fox (and Build a Dog),* but suffice it to say that the tame foxes today are even friendlier and more affectionate toward humans. They inherently follow human gazes and gestures, and they look ever more eerily doglike—adding rounder snouts and shorter, chunkier limbs to their other characteristics.

With advances in genetics, our team has in recent years been able to probe the process of domestication at the DNA level. Many, but certainly not all, of the chromosomal regions of genetic change associated with the unique behavioral and morphological characteristics of the tame foxes have been mapped onto fox chromosome number 12. In particular, we uncovered on chromosome 12 a number of quantitative trait loci (QTLs)—stretches of DNA associated with genes underlying continuously varying traits that are linked to tame behavior. (In humans, examples of varying traits associated with QTLs include height and skin color.)

By comparing these DNA sequences with what was known about the genetics of domestication in dogs, Anna Kukekova, I and our colleagues were able to confirm that in many cases the QTLs on fox chromosome 12 were similar to QTLs involved in the domestication of dogs. We thus conclude that, through selective breeding over dozens of generations, we have loosely replayed the transformation of a wild canid to a house pet at the genetic level.

The foxes are even starting almost literally to tell us things. When Svetlana Gogoleva and I analyzed the vocalizations of tame foxes versus those of aggressive foxes, we found that the sounds made by the tame foxes are unique. The acoustic dynamics of their vocalization are remarkably similar to human laughter. We do not know how or why the tame foxes "laugh," but a more pleasant way for one species to bond with another is hard to imagine. SA

MORE TO EXPLORE

Animal Evolution during Domestication: The Domesticated Fox as a Model. Lyudmila Trut et al. in *Bioessays,* Vol. 31, No. 3, pages 349–360; March 2009.

How to Tame a Fox (and Build a Dog): Visionary Scientists and a Siberian Tale of Jump-Started Evolution. Lee Alan Dugatkin and Lyudmila Trut. University of Chicago Press, 2017.

FROM OUR ARCHIVES

From Wolf to Dog. Virginia Morell; July 2015.

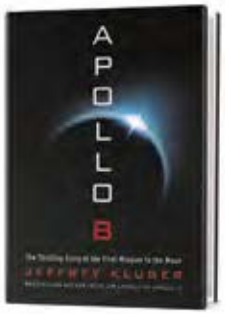
scientificamerican.com/magazine/sa

RECOMMENDED

By Andrea Gawrylewski

Apollo 8: The Thrilling Story of the First Mission to the Moon

by Jeffrey Kluger. Henry Holt, 2017 ($30)

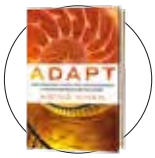


EARTH RISES over the lunar surface in a 1968 photograph (*shown in its original orientation*) by the *Apollo 8* astronauts.

In the summer of 1969 Neil Armstrong and Buzz Aldrin took humanity's first steps onto the lunar surface during NASA's *Apollo 11* mission. Yet an arguably more epochal event occurred the previous year, when the crew of *Apollo 8*—astronauts Frank Borman, Jim Lovell and Bill Anders—embarked on the first voyage to lunar orbit. Their flight was also the first time that human beings escaped Earth's gravity and, with its live television broadcast from around the moon, the first time that billions of people on Earth witnessed their home planet from a cosmic perspective. Kluger, a science journalist, previously co-authored the best-selling book turned blockbuster film *Apollo 13*, and his latest foray into space history overflows with similarly cinematic details. *Apollo 8* delivers the definitive story of what is, and always will be, one of humanity's greatest adventures. —*Lee Billings*

Adapt: How Humans Are Tapping into Nature's Secrets to Design and Build a Better Future

by Amina Khan. St. Martin's Press, 2017 ($26.99)



Imagine military combat gear that automatically changes color to match its surroundings, from desert to snowy tundra. This is one of the goals of researchers looking to the natural world to improve on human design and innovation. For the combat gear, scientists are studying the pigments in cuttlefish that change to blend in with the fish's background. Science writer Khan walks readers through other examples: Snakes and the physics of slithering, which might help engineers design new probes; and termites, whose towering mud nests could inspire next-generation architecture. Biomimicry, as the design philosophy is known, could generate some $1 trillion in goods and services globally and help to solve environmental and health problems, Kahn reports. But to make it work, we must first understand the wondrous evolutionary adaptations of the natural world.

Scienceblind: Why Our Intuitive Theories about the World Are So Often Wrong

by Andrew Shtulman. Basic Books, 2017 ($30)

It is nothing new that some people are distrustful of science. Shtulman, a professor of cognitive science and psychology, points out that this skepticism arises from many sources: political and religious beliefs, cultural identity, as well as our own intuitive, inborn theories. Such theories help even babies intuit basic concepts of matter and motion. But they also lead us down incorrect lines of reasoning—the earth is flat because we can't see the ground curve around us, for instance. Shtulman shows how the intuitive theories of the physical and biological world can blind us to science. Consider the innate theory that a bullet shot from a gun will hit the ground later than a bullet simultaneously dropped straight down. Repeated physics experiments show they hit at the same time, one of many examples of, as the author calls it, the triumph of evidence over intuition.

Finding Fibonacci: The Quest to Rediscover the Forgotten Mathematical Genius Who Changed the World

by Keith Devlin. Princeton University Press, 2017 ($29.95)

Mathematicians developed the familiar 10-digit numerical system, known as the Hindu-Arabic numerals, over the course of centuries. One man, however, helped to bring that system to the West. His name was Leonardo of Pisa, although we know him better as Fibonacci. Leonardo's 1202 *Book of Calculation* popularized the Hindu-Arabic numerals by teaching Italian merchants to do arithmetic without the abacus. Devlin's account is as much about his own quest to reveal the mathematician's legacy as it is about Leonardo himself. The author, a Stanford University mathematician, talks his way into Italian research libraries in search of early manuscripts, photographs all 11 street signs on Via Leonardo Fibonacci in Florence and strives to cultivate a love for numbers in his readers. —*Andrea Marks*

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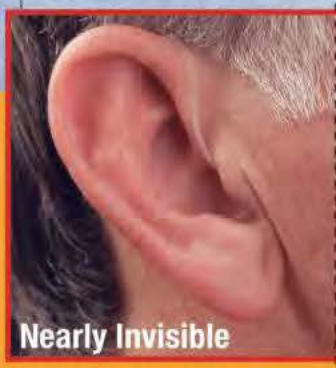

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Michael Shermer is publisher of *Skeptic* magazine (www.skeptic.com) and a Presidential Fellow at Chapman University. His next book is *Heavens on Earth.* Follow him on Twitter @michaelshermer

On Witches and Terrorists

Why torture doesn't work

By Michael Shermer

As recounted by author and journalist Daniel P. Mannix, during the European witch craze the Duke of Brunswick in Germany invited two Jesuit scholars to oversee the Inquisition's use of torture to extract information from accused witches. "The Inquisitors are doing their duty. They are arresting only people who have been implicated by the confession of other witches," the Jesuits reported. The duke was skeptical. Suspecting that people will say anything to stop the pain, he invited the Jesuits to join him at the local dungeon to witness a woman being stretched on a rack. "Now, woman, you are a confessed witch," he began. "I suspect these two men of being warlocks. What do you say? Another turn of the rack, executioners." The Jesuits couldn't believe what they heard next. "No, no!" the woman groaned. "You are quite right. I have often seen them at the Sabbat. They can turn themselves into goats, wolves and other animals.... Several witches have had children by them. One woman even had eight children whom these men fathered. The children had heads like toads and legs like spiders." Turning to the flabbergasted Jesuits, the duke inquired, "Shall I put you to the torture until you confess?"

One of these Jesuits was Friedrich Spee, who responded to this poignant experiment on the psychology of torture by publishing a book in 1631 entitled *Cautio Criminalis,* which played a role in bringing about the end of the witch mania and demonstrating why torture as a tool to obtain useful information doesn't work. This is why, in addition to its inhumane elements, it is banned in all Western nations, including the U.S., whose Eighth Amendment of the Constitution prohibits "cruel and unusual punishments."

What about waterboarding? That's "enhanced interrogation," not torture, right? When the late journalist Christopher Hitchens underwent waterboarding for one of his *Vanity Fair* columns, he was forewarned (in a document he had to sign) that he might "receive serious and permanent (physical, emotional and psychological) injuries and even death, including injuries and death due to the respiratory and neurological systems of the body." Even though Hitchens was a hawk on terrorism, he nonetheless concluded: "If waterboarding does not constitute torture, then there is no such thing as torture."

Still, what if there's a "ticking time bomb" set to detonate in a major city, and we have the terrorist who knows where it is—wouldn't it be moral to torture him to extract that information? Surely the suffering or death of one to save millions is justified, no? Call this the Jack Bauer theory of torture. In the hit television series *24,* Kiefer Sutherland's character is a badass counterterrorism agent whose "ends justify the means" philosophy makes him a modern-day Tomás de Torquemada. In most such scenarios, Bauer (and we the audience) knows that he has in his clutches the terrorist who has accurate information about where and when the next attack is going to occur and that by applying just the right amount of pain, he will extort the correct intelligence just in time to avert disaster. It's a Hollywood fantasy. In reality, the person in captivity may or may not be a terrorist, may or may not have accurate information about a terrorist attack, and may or may not cough up useful intelligence, particularly if his or her motivation is to terminate the torture.

In contrast, a 2014 study in the journal *Applied Cognitive Psychology* entitled "The Who, What, and Why of Human Intelligence Gathering" surveyed 152 interrogators and found that "rapport and relationship-building techniques were employed most often and perceived as the most effective regardless of context and intended outcome, particularly in comparison to confrontational techniques." Another 2014 study in the same journal—"Interviewing High Value Detainees"—sampled 64 practitioners and detainees and found that "detainees were more likely to disclose meaningful information ... and earlier in the interview when rapport-building techniques were used."

Finally, an exhaustive 2014 report by the Senate Select Committee on Intelligence analyzed millions of internal CIA documents related to the torture of terrorism suspects, concluding that "the CIA's use of its enhanced interrogation techniques was not an effective means of acquiring intelligence or gaining cooperation from detainees." It adds that "multiple CIA detainees fabricated information, resulting in faulty intelligence."

Terrorists are real. Witches are not. But real or imagined, torture doesn't work. SA

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Illustration by Izhar Cohen

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SPEAKERS:

John D. Barrow, FRS

John D. Barrow, FRS is Professor of Mathematical Sciences at Cambridge University and Director of the Millennium Mathematics Project, an outreach program for students and the general public. He studies cosmology and the interface between particle physics and astronomy. He is well known for his work on the Anthropic Principles in cosmology as well as the study of the large-scale structure and early history of the universe, and studies of whether the constants of Nature might be changing in time. He has also written and lectured extensively on the applications of mathematics to sport and the arts. Dr. Barrow has received many awards; he is a Fellow of the Royal Society and a member of the Academia Europaea, and holds five honorary doctorates. He has written more than 500 scientific papers, and 22 books translated into 28 languages. His play, *Infinities*, won the Premi Ubu for best play in the Italian theatre in 2002 and the 2003 Italgas Prize.

Bernie Carlson, Ph.D.

Bernie Carlson is the Joseph L. Vaughan Professor of Humanities at the University of Virginia. He is also Chair of the Department of Engineering and Society and holds a joint appointment in UVa's History Department. As a historian of technology, Dr. Carlson has written widely on invention and entrepreneurship as well as on the role of technology in the rise and fall of civilizations. He has written numerous books, including *Tesla: Inventor of the Electrical Age*, which has been translated into nine languages and won several awards. Dr. Carlson has also filmed 36 lectures on *Understanding the Inventions that Changed the World* for The Great Courses. He directs Engineering Business Programs at UVa and teaches a course called Engineers as Entrepreneurs. For over a decade, he was a consultant on innovation to Corning Incorporated and has served on several governing boards. He recently finished a five-year term as Executive Secretary for the Society for the History of Technology.

Robert Garland, Ph.D.

Robert Garland is the Roy D. and Margaret B. Wooster Professor of the Classics at Colgate University. In addition to his 30 years teaching Classics at Colgate University, Robert Garland has taught English and Drama to secondary school students and lectured at universities throughout Britain and at the British School at Athens. Before beginning his Ph.D. he trained professionally as an actor and has directed a number of plays. His research focuses on the social, religious, political, and cultural history of both Greece and Rome. He has written 13 books and many articles in both academic and popular journals. His expertise has been featured in The History Channel's *The True Story of Troy*, and he has often served as a consultant for educational film companies. Dr. Garland has taught *Greece and Rome: An Integrated History of the Ancient Mediterranean*, *The Other Side of History*, and *Living History* for The Great Courses. He is an avid squash player and cyclist.

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Stephen Ressler, Ph.D.

Stephen Ressler is Professor Emeritus from the United States Military Academy at West Point and a Distinguished Member of the American Society of Civil Engineers (ASCE). He served for 34 years as a commissioned officer in the U.S. Army Corps of Engineers and retired at the rank of Brigadier General in 2013. In 2007, he deployed to Afghanistan to create a civil engineering program for the newly created National Military Academy of Afghanistan in Kabul. Dr. Ressler is passionate about communicating the joys of engineering to inquiring minds of all ages. His three video lecture series — *Understanding the World's Greatest Structures, Understanding Greek and Roman Technology*, and *Everyday Engineering* — are among the most highly-rated offerings in The Great Courses' catalog. Dr. Ressler has received numerous awards and his Bridge Designer software has been used by over two million students worldwide. He is also a developer and principal instructor for the ASCE Excellence in Civil Engineering Education Teaching Workshop.

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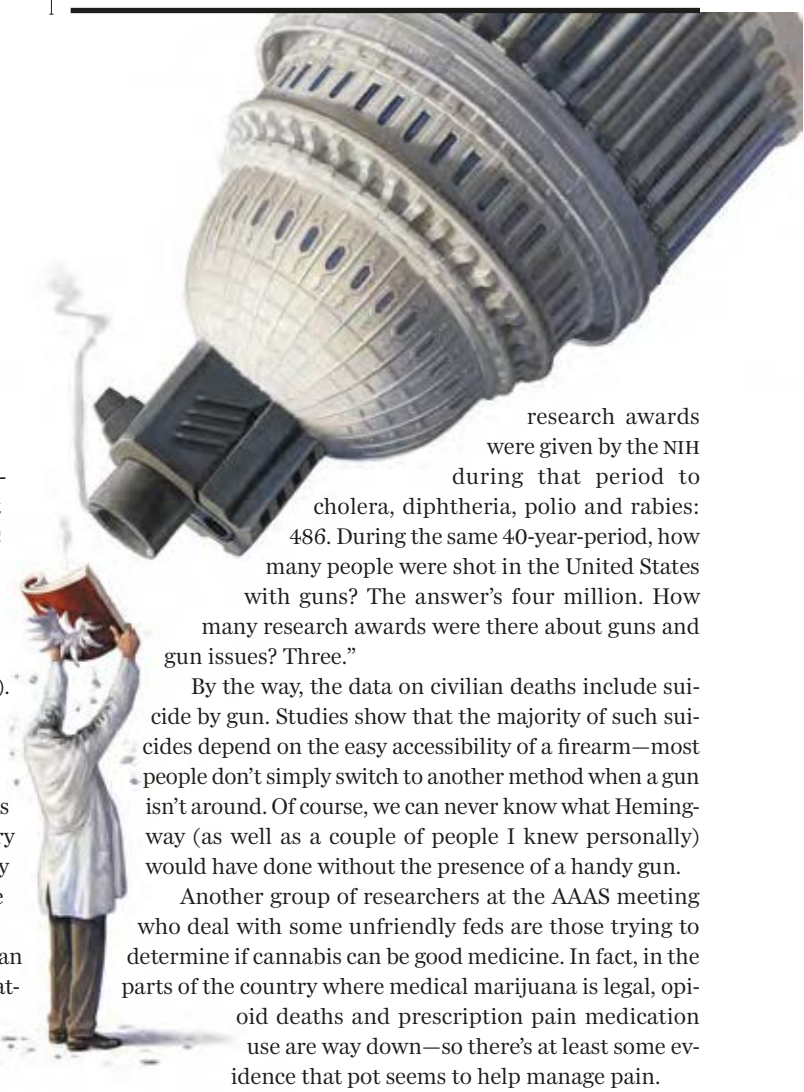
Steve Mirsky has been writing the Anti Gravity column since a typical tectonic plate was about 36 inches from its current location. He also hosts the *Scientific American* podcast Science Talk.

Don't Pass the Weed or Say "Guns"

Feds frustrate researchers trying to study pistols and pot

By Steve Mirsky



Ernest Hemingway, Nobel laureate in literature, wrote *A Farewell to Arms*. David Hemenway, professor of health policy at the Harvard T. H. Chan School of Public Health, wishes CDC personnel could just mention arms. "Researchers, staff at the Centers for Disease Control, are afraid to say the word 'guns' or 'firearms,'" Hemenway said on February 17 at a session on gun-violence research at the annual meeting of the American Association for the Advancement of Science (AAAS). The conference took place in Boston, famous for gun-related havoc since the Boston Massacre (which, unlike the Bowling Green Massacre, actually happened).

"Public health is underfunded relative to medicine in terms of research," Hemenway noted. "Within public health, injury prevention is particularly underfunded. And within injury prevention, firearms research is the most underfunded for the size of the problem."

According to Hemenway, on average in the U.S., more than 300 people get shot daily. A third of them die. "Since I graduated from college [in 1966], there have been more civilian deaths from guns in the United States than combat deaths on the battlefield in all the wars in United States history, including the Civil War and World War II." (And, of course, the war that started brewing after the Boston Massacre.)

"Twenty years ago [the CDC was] doing a tiny amount of funding for firearms research … $2.6 million a year total," Hemenway said. "This was too much for the gun lobby and Republicans in Congress, and they attacked the CDC. And now the CDC does no funding of firearms research. Zero."

No official prohibition stops the CDC from offering such funding. But Hemenway says that CDC folks avoid even saying "guns" or "firearms" to keep out of congressional crosshairs: "The director of the CDC, of our major public health agency, we've had mass shooting after mass shooting in the United States, and what has he said? And I don't blame him … not a single word. And for good reason. Because he knows if he says anything about guns, funding will be cut." Talk about trigger warnings.

The National Institutes of Health also feels the chill of a congressional freeze-out. Hemenway talked about research that examined grants given by the NIH during a 40-year period. "How many deaths were from cholera, diphtheria, polio and rabies in the United States? And the answer was 2,000. How many research awards were given by the NIH during that period to cholera, diphtheria, polio and rabies: 486. During the same 40-year-period, how many people were shot in the United States with guns? The answer's four million. How many research awards were there about guns and gun issues? Three."

By the way, the data on civilian deaths include suicide by gun. Studies show that the majority of such suicides depend on the easy accessibility of a firearm—most people don't simply switch to another method when a gun isn't around. Of course, we can never know what Hemingway (as well as a couple of people I knew personally) would have done without the presence of a handy gun.

Another group of researchers at the AAAS meeting who deal with some unfriendly feds are those trying to determine if cannabis can be good medicine. In fact, in the parts of the country where medical marijuana is legal, opioid deaths and prescription pain medication use are way down—so there's at least some evidence that pot seems to help manage pain.

But marijuana is still what is known as a Schedule I substance—the Food and Drug Administration does not recognize a legitimate medical use for it, so scientists have to jump through flaming hoops to get any to study.

"It can't come off of Schedule I to a different schedule until the traditional drug development work has been done, and I don't think the traditional drug development work [large phase III trials] really can be done while it's Schedule I," said Ryan Vandrey of the Johns Hopkins University School of Medicine on February 19 at the AAAS conference. "It's a catch-22."

And it's not likely to be uncaught any time soon, especially with Jeff Sessions as attorney general (he still was as we went to press, anyway). In April 2016 Sessions famously said, "Good people don't smoke marijuana," which is so vacuously, reductively absurd as to render a retort unnecessary. Except for the one I saw on Twitter reacting to the Sessions quote: "True. I eat it." SA

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Illustration by Matt Collins

50, 100 & 150 YEARS AGO

INNOVATION AND DISCOVERY AS CHRONICLED IN *SCIENTIFIC AMERICAN*

Compiled by Daniel C. Schlenoff

MAY

1967 Nuclear Power

"By the year 2030 the electric power requirement will be 10 times the present capacity. Because of the expected decline in fossil-fuel resources, and in the absence of any other large source of energy at reasonable cost, fission power would be counted on to supply about 85 percent of this need. To fill such a demand with fission plants of the present type, however, would call for quantities of uranium ore that would soon deplete reserves. Thus, the fission age would be over almost before it began. These facts make plain how heavily the 'fission age' (perhaps to be followed someday by a 'fusion age') can depend on success in developing power plants with breeder reactors that will make the most of the available resources."

Matter

"Thales of Miletus, the first philosopher, is said to have asked, 'How, and of what, is the world made?' Perhaps in retrospect the fact that some of the laws governing atoms are different from those apparently governing bulk matter should not have been so surprising as it was. As we have seen, Democritus already realized that the components of matter were substances different from matter itself. The nuclear atom of Ernest Rutherford and Niels Bohr, as described by quantum theory, proved sufficient, as it has been said, to account for all of chemistry and most of physics."

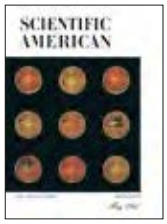
1917 Making Movies

"With all outdoors for its stage and with nature as the scene painter, the motion picture will always possess a tremendous advantage over the legitimate drama which must necessarily confine even its most grandiose efforts to a comparatively limited stage and artificial scenery. Realizing this full well, the motion picture director works largely in the open, and when a story justifies the expense and trouble, he does not hesitate to gather an army of players and make use of a natural stage whose dimensions are measured not in feet but in miles. Big scenes are rather the exception than the rule in motion picture productions, for they are exceedingly costly."

Archive images of the art and science of moviemaking from 1917 are at www.ScientificAmerican.com/may2017/movies-1917

Darwinism and War

"Mr. Chalmers Mitchell's new book, 'Darwinism and War' is a reply to the argument in favor of war, so often put forth in the last three years by a certain German school, that a state of constant struggle or warfare is a dominant factor in evolution. These writers declare that war is both necessary and admirable, and is in fact a biological law which man cannot resist, and that it is, moreover, beneficial in the long run, favoring the survival of the strongest and ablest races. Mr. Mitchell finds, however, in his own words: 'Natural selection results from the conservation of favored races rather than from the extermination of one race by another.' He finds nothing in common between the grouping of individuals which forms a modern nation and that which constitutes a race or species of animals. In short he believes it is entirely inadmissible to attempt to justify human conduct by laws supposed to be dominant in the animal kingdom."



1967

1917


1867


1917: Movie magic takes to the great outdoors: plenty of ambition and extras—and the world for a stage.

1867 Gunshot Wounds

"Dr. V. Gelcich of Los Angeles, Calif., says that there is much difficulty in discriminating between bone and the ball by the use of the ordinary probe. His probe is simply a piece of white pine wood, made in the shape of a probe, introduced into the wound, rubbed against the suspected object, and quickly withdrawn when, if it has touched the ball, traces of lead will be found upon it. He says, by this simple instrument, while a medical officer in the United States Army, he saved the limbs of two men on whom amputation was about to be performed for gunshot wounds in the lower extremities; what was long supposed to be bone proving to be lead by the aid of the white pine probe."

Parisian Horsepower

"A French way of riding on horseback: make a pair of enormously large wheels, and place a carriage body over the axle and shafts so high that the horse can travel under it and between the wheels. You will have a most symmetrical turn-out, such as they use in Paris, of driver, horse and carriage in one, and a lofty perch where you can both see and be seen."

SCIENTIFIC AMERICAN, VOL. CXVI, NO. 18; MAY 5, 1917

The Elusive Northwest Passage

Arctic route may remain treacherous for decades

As sea ice in the warming Arctic retreats more and more during summer, the fabled Northwest Passage is becoming a greater temptation. The route—actually a series of straits across northern Canada—would cut 3,000 miles off the voyage from New York City to Shanghai via the Panama Canal. But in practice, lingering ice is so unpredictable that a crossing remains risky and expensive. Arctic scientists think it will be many years before ships can make the passage regularly. —*Katie Peek*

Ocean to Ocean

Two high-profile crossings

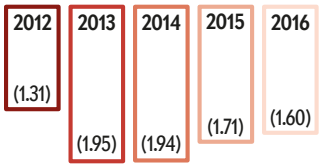
Nunavik (2014)

Crystal Serenity (2016)

As many as 30 ships have traversed the Northwest Passage each summer since 2007 (the straits are ice-locked in winter). In 2014 the Canadian ship *Nunavik* was the first cargo vessel to cross without icebreaker accompaniment. Last summer *Crystal Serenity* from France became the first giant cruise ship to undertake the voyage.

Year by Year

Extent of ice in September
(annual minimum, million square miles)



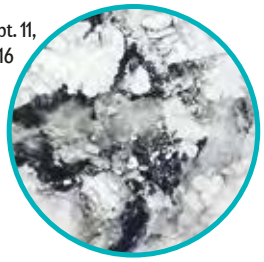
Ice cover varies annually. An open-water path through the passage was easier to find in 2012 and 2016, but in 2013 and 2014 the routes were relatively icy. The variability foils long-term planning for navigators.

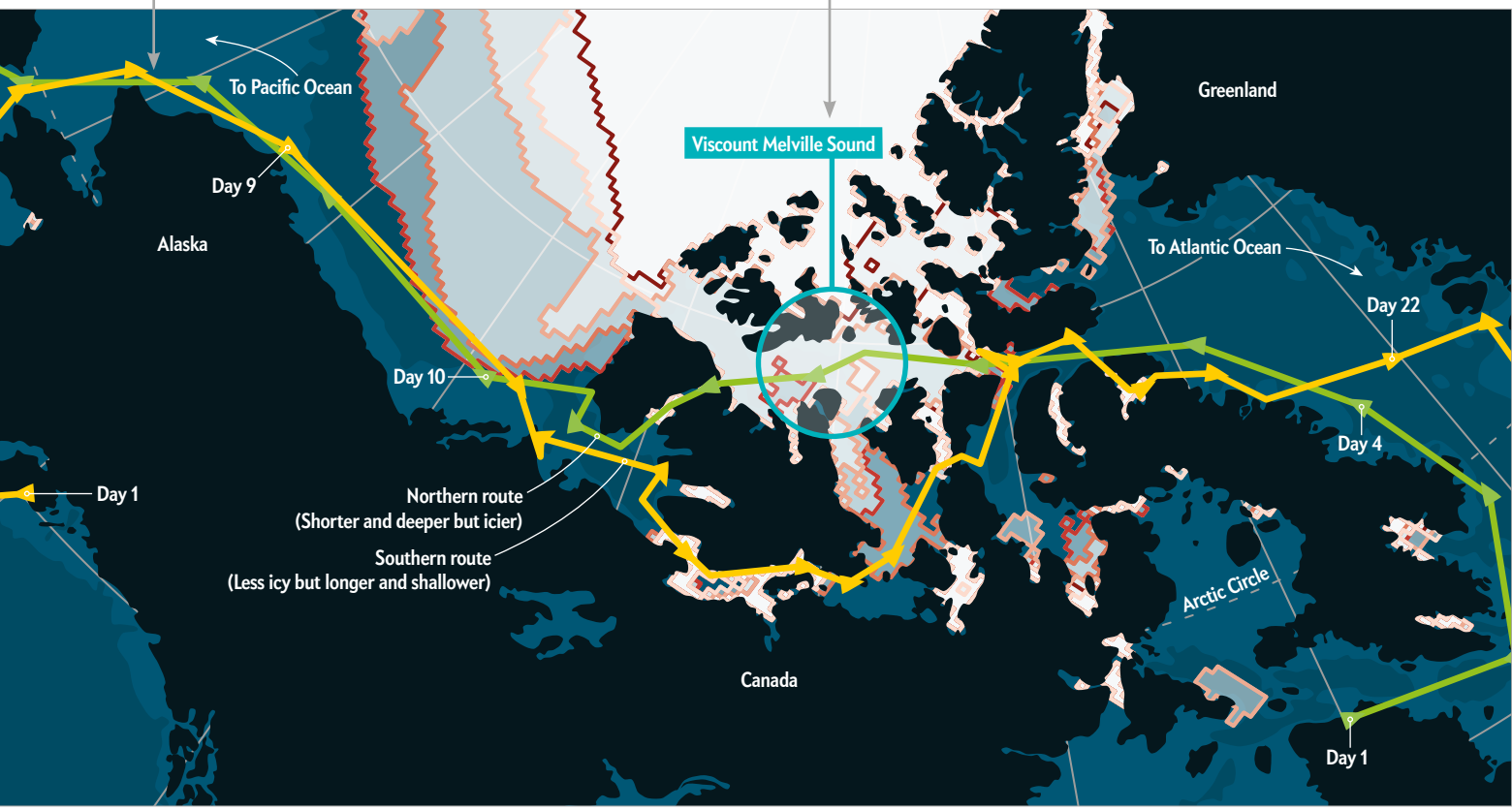
Week by Week

Ice that breaks off from the polar cap is old and solid, and even ships with reinforced hulls avoid it. If these icebergs drift into choke points, such as the Viscount Melville Sound, it may be days before the passage clears. And because navigational charts in the region are spotty, ships often cannot change routes on the fly. Instead they wait.

Aug. 27, 2016

Sept. 11, 2016





COURTESY OF NASA WORLDVIEW (*satellite images*); SOURCES: U.S. NATIONAL SNOW AND ICE DATA CENTER (*annual ice extents*); CANADIAN ICE SERVICE (*Viscount Melville Sound*); FEDNAV (Nunavik); CRYSTAL CRUISES (Crystal Serenity)

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