DISEASE FACTORIES
Why the government won't stop the problem at pig farms

What our stories say about our prehistoric past
THE EVOLUTION OF MYTHS

BIRTH OF OUR SOLAR SYSTEM
A (surprisingly violent) blur of collisions

Is carbon from permafrost speeding up climate change?
AS THE TUNDRA THAWS

SCIENTIFIC AMERICAN

10 IDEAS
THAT WILL CHANGE THE WORLD

INSIDE

A BATTERY THAT EATS CARBON

CLOTHES THAT COOL

PREDICTING POVERTY

THE (UNHACKABLE) QUANTUM INTERNET

SUPERMATERIALS FROM SUPERATOMS

A SHIELD AGAINST VIRUSES

ANTIBIOTICS FROM SCRATCH

SOFTWARE THAT CAN READ

ROBOT IN A PILL

BLOOD TESTS AS CHEAP AS PAPER

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DECEMBER 2016

VOLUME 315, NUMBER 6

ON THE COVER

While facts, reason and human progress have not exactly been front and center for the past year, in this issue we offer our annual roundup of early-stage scientific advances with potential to solve big problems and improve life for people everywhere. The 2016 edition of World Changing Ideas begins on page 32.

Image by Kenn Brown, Mondolithic Studios.

Photograph by Patrick Cavan Brown

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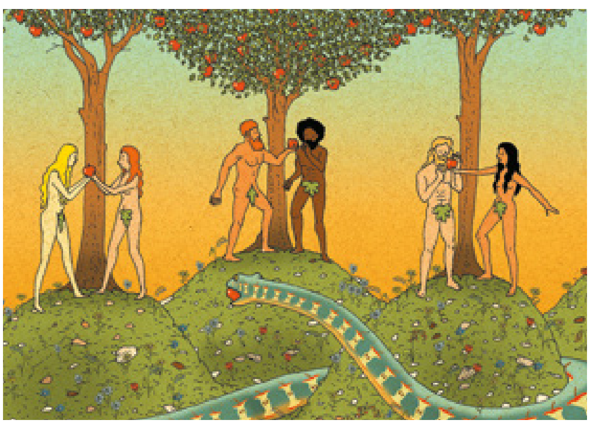
10

18



84

ON THE WEB

Cosmic Conundrum
Scientific American explores physicists' efforts to understand the quantum nature of spacetime.
Go to www.ScientificAmerican.com/dec2016/spacetime

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

Ideas to Change the World

It's no secret we at *Scientific American* are fans of the kinds of bold ideas that can help take humanity to a better future. Recently technology, especially digital, seems to be advancing more swiftly than ever. Noting the trend, even the policy leaders at the World Economic Forum's Davos meeting this year focused on the theme of the "Fourth Industrial Revolution."

How do you know what emerging technologies are likely to make the most difference? We make our annual bets in the cover story, "World Changing Ideas," starting on page 32. Among the 10 advances we discuss are those that could ease poverty through the use of machine-learning software and satellites, could reduce energy consumption while capturing carbon, and could maybe even kill viral infections once and for all.

Of course, a bane of any given technology is its misapplication. Consider antibiotics, the "wonder drugs" that conquered bacterial infections for decades. Resistant bacteria are rising today, largely thanks to our profligate use of these medicines, particularly on farms. The drugs keep animals in crowded conditions both healthier and able to grow faster on less food. As Melinda Wenner Moyer explains in "The Looming Threat of Factory-Farm Superbugs," the frightening result is a cauldron of fast-spreading trouble, including methicillin-resistant *Staphylococcus aureus* (MRSA). Turn to page 70 for more.

Improving human welfare doesn't have to rely on technology. Sometimes we just have to incorporate what research has already shown into our society's policies. Politicians often speak abstractly about their support for families, for instance, but in this issue we propose a concrete solution: paid parental leave. In our Science Agenda, "Bringing Up Baby, Helping the Economy," on page 10, we explain how studies show that paid leave results in healthier children and less stressed parents, without hurting businesses. The U.S., however, is the only developed nation that does not guarantee it.

Although all our Science Agenda columns represent the editorial team's collective perspective, this one resonates with me more personally than usual. I had my first daughter two decades ago, when my husband and I were just able to cover our household expenses. Because I then had 10 years' tenure at a previous employer, I was able to cobble together almost six weeks of paid "vacation" time to stay home (too briefly) after her birth, so we had no income gap. I vividly remember my feeling of shock that the U.S. had not figured out such seemingly simple matters. Still, I counted myself lucky. New parents shouldn't have to count on luck. Put simply, when conditions are better for families with infants, humanity's future is brighter as well. SA

Illustration by Kenn Brown, Mondolithic Studios (test-tube globe), Illustration by Nick Higgins (DiChristina)

[**inside**view]

THINKING ABOUT THINKING: ALZHEIMER'S DISEASE RESEARCH

A conversation with BRANDY MATTHEWS, MD, Senior Medical Advisor, Alzheimer's Disease Team, Eli Lilly and Company

Developing new therapies for Alzheimer's disease is hard—so hard, in fact, that many large pharmaceutical companies have abandoned the pursuit. But not Eli Lilly and Company. With nearly 50 million people worldwide living with the devastating disease, the Indianapolis-based drug maker has doubled down on its effort to find treatments that halt the progression of Alzheimer's and reduce its burden on patients, caregivers and society. Brandy Matthews, a senior medical advisor on the Alzheimer's disease team at Lilly, explains why the company remains so dedicated to the cause.

Given the checkered history of Alzheimer's drug research, how do you expect to succeed where so many others have failed?
Alzheimer's is such a complex disease that perseverance is the name of the game. Research isn't only about successes. It's about what we can learn when we don't succeed. By analyzing findings from our studies, as well as those conducted by other industry and academic institutions we gain insights that help us continuously refine our clinical development program. Our current pipeline is shaped by the discoveries we've made over the past three decades. We have compounds that target both beta-amyloid and tau—two known hallmarks of the disease—along with positron emission tomography (PET) imaging diagnostics that allow researchers to see both pathologies in the living brain.

PERSEVERANCE IS THE NAME OF THE GAME

Through perseverance, we are hopeful that one day there will be a solution for the many individuals living with Alzheimer's disease.

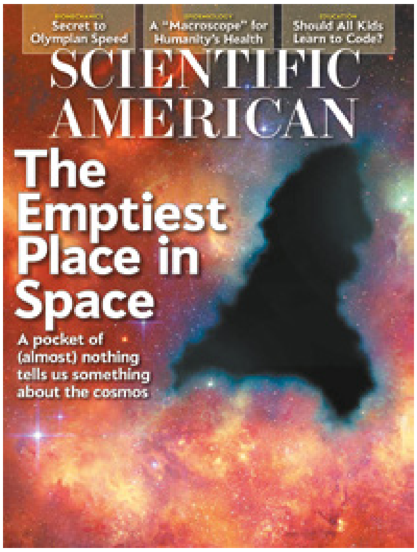
What is the focus of your work as a senior medical advisor?
My responsibility is to interpret the science that's generated by our researchers here at Lilly and by other leaders in the field of Alzheimer's disease. I then explain the implications of that science to my colleagues, healthcare professionals, advocacy organizations, patients and caregivers. This role is a unique fit that's well suited to my skillsets. In my academic career, I was both an educator and a clinician. With that background, I understand the complicated science, but I can also accurately distill it down and communicate it on the level of an individual patient.

Why did you decide to leave your position as an associate professor of clinical neurology and join Lilly?
During my academic career, I used to recruit patients into clinical trials. As I got to know them, I would reassure them that there were all these brilliant scientists working day and night to find some relief for their disease. Then one day I had an epiphany: Instead of talking about those scientists, I could join their ranks. My academic career was very intellectually stimulating and fulfilling, but Lilly offered me a chance to potentially impact the lives of millions of people without ever leaving my hometown.

What led you to become a neurologist and to focus on Alzheimer's in the first place?
I didn't start on the path to medicine as a young person. I thought I'd be a vocalist or an actress. But the summer after I completed my undergraduate degree, I discovered two life-changing books. One was about synesthesia — a condition in which the senses become mixed, so tasting shapes, seeing music, that sort of thing. The other was a philosophical novel that emphasized the primacy of reason. Together, those books convinced me that I should spend my time thinking about thinking. So, I went down this 15-year path to become a behavioral neurologist. I am still involved in patients' human stories, which originally drew me to performance, but because I investigate neurodegenerative disorders that affect cognition, I also get a window into the mind. It's a natural fit.

What continues to motivate you to find a therapy that can halt patient decline?
Given the state of the science, I believe that we have an opportunity to make Alzheimer's disease, as we like to say around here, a distant memory—and to do so within my professional lifetime. To find a medicine that can modify the course of this disease, one that's delivered to the right patients at the right time, could change the lives of millions of individuals. For me, there is no stronger motivation.

Lilly



August 2016

PROGRAMMING FOR ALL

In "The Coding Revolution," Annie Murphy Paul reports on discussions and initiatives related to teaching computer science to all public school students, with a distinction made between coding and "computational thinking," which is described as "habits of mind that include breaking down a problem, designing systems, and running small experiments."

Enough hand-wringing, please! From my experiences as a teacher and a former senior adviser to the Commonwealth of Virginia for STEM initiatives, I can say that while certain areas of computer literacy are required for today's students, in general they don't need a deeper than basic understanding of how computers work any more than they need a mechanic's knowledge of how a car works to prepare for driving. All students do need some fundamental *programming* skills, and those planning on a STEM major in college would benefit from an introduction to computational methods for science and engineering. But to get tied up in deep angst about such issues as computational thinking and to talk about a massive involvement of such thinking in all disciplines will stall any implementation of appropriate levels of computer literacy in grades K–12 for many years as focus groups are created, data taken and reports written.

Jim Batterson
via e-mail

"Students in general do not need a deeper than basic understanding of how computers work any more than they need a mechanic's knowledge of how a car works."

JIM BATTERSON *VIA E-MAIL*

In the social and medical fields, a researcher has to demonstrate that there is empirical evidence supporting that an intervention may work and that he or she has thought through all possible harms that may accrue before experimenting on humans (or even animals). In education, though, it seems as if we can introduce an intervention that affects tens of thousands of students simply on the basis that it seems to make sense. We have seen disastrous effects from such massive educational experiments, such as teaching set theory instead of basic mathematical skills.

The rationale given in Murphy Paul's article for teaching computational thinking is that it fosters other skills, such as "a flexible set of mental tools." Similar arguments were given more than a century ago for teaching penmanship and Latin. But in 1913 this was proved to be wrong by psychologist Edward Thorndike, who concluded that "a change in one function alters another only in so far as the two functions have as factors identical elements."

David L. Streiner
Department of Psychiatry and Behavioral Neurosciences
McMaster University, Ontario

It's nice to see what was called "critical thinking" is now being promoted in elementary and secondary schools. It is better to teach the concepts of programming via computational thinking than to focus on teaching kids to write code. The teaching methods for such computational thinking sound very similar to those I used in a general education class that I taught at the University of Arizona in the late 1980s and the early 1990s. Early on, I realized that teaching the particular subject matter was not the purpose of the course. Rather it was to teach critical thinking to students who, for the most part, relied on the rote memorization they had been drilled in while in their elementary and secondary schools.

Kenneth C. Young
Petrolia, Calif.

ASTEROID MISSION

"The Seven-Year Mission to Fetch 60 Grams of Asteroid," by Dante S. Lauretta, states that the "safest regions" of the asteroid Bennu for NASA's OSIRIS-REx spacecraft to visit "will likely be near the equator, where the spacecraft can more easily match the velocity of the spinning asteroid to touch down on the surface."

I would think that the easiest spots to land on or hover over would be at the poles, especially if the spin rate of the asteroid is fairly high.

Steve Murphy
Cody, Wyo.

LAURETTA REPLIES: For a spacecraft to safely make contact with a spinning asteroid, it must match the transverse velocity of the surface, which is greatest at the asteroid's equator and drops to zero at its poles. One would thus think that touching down at a pole would be easiest for OSIRIS-REx, but this is not so for a number of reasons.

Most important, the scientific requirements for the illumination of the touch-and-go (TAG) site are not met. The site must have a solar phase angle of more than 85 degrees, and Bennu's pole is closely aligned with the ecliptic plane, which makes that impossible.

Another constraint is imposed by the fact that the spacecraft departs for TAG from an orbit in the terminator plane, which means that the desire for the TAG transfer trajectory to be four hours and for the checkpoint maneuver that initiates descent to the surface to be near periapsis is much harder to fulfill for polar sites.

For meeting the TAG contact velocity requirements, there are some sites that are more challenging than others, but variations in topographic features in the site's vicinity and in the terrain that is overflown *during the approach to it have the largest effect on TAG dynamic performance.*

HEAD BUG

In "Zombie Neuroscience," Christie Wilcox describes how jewel wasps attach eggs to cockroaches so that their offspring can devour them alive, which involves injecting dopamine into the cockroaches' brain.

Wilcox could have further elaborated on an imagined cockroach's nightmares before and after the dopamine loading. Rather than sensing horror, it could instead feel the approach of a hijack wasp as the ultimate emotional high, despite ensuing certain death.

Jožko Strauss
via e-mail

SUPERVOID

In "The Emptiest Place in Space," István Szapudi explains that because of the accelerating expansion of the universe, photons experience a net loss of energy as they traverse a supervoid, a very large expanse of space with relatively little matter or galaxies. If this phenomenon is not to violate the law of conservation of energy, then where does the photons' energy go?

Thomas Luckett
Portland, Ore.

Szapudi says the cosmic microwave background (CMB) can be observed by tuning an old TV between channels. But unless the TV's signal detector is cryogenically cooled to extremely low temperatures, the thermal noise of the detector will overwhelm the CMB, making it impossible to observe.

John J. Carroll
Indianapolis, Ind.

SZAPUDI REPLIES: In answer to Luckett's question: The photon is not a closed system; it interacts with the expanding universe, and the expanding universe takes up the excess energy from the photon. This is why it does not regain the full energy it originally had before starting to cross the changing potential of the supervoid.

Regarding Carroll's letter: It has been estimated that about 1 percent of the "snow" in analog TV static comes from CMB radiation. This signal to noise is small but nonnegligible, and it isn't a stretch to call it an observation.

LETTERS TO THE EDITOR

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Bringing Up Baby, Helping the Economy

Paid parental leave produces healthier children and businesses

By the Editors

Too often new parents feel terrified—and not just about the daunting prospect of raising a child. Many of them must grapple with a gut-wrenching decision: How quickly can they leave their newborn to get back to their job? Few can afford to go without salaries for long or to weaken their future wage-earning potential by leaving their job altogether.

Americans face such dilemmas because 88 percent of the private U.S. workforce is ineligible for paid family leave. As a result, many women and men clock back in to work within weeks. The cost of that decision can be measured in poorer health outcomes for their newborn and for themselves.

Right now the U.S. holds the dubious honor of being the only developed nation without policies guaranteeing parents a temporary paid leave from their job. Even countries with fewer resources offer better policies: in Costa Rica, for example, mothers receive full pay if they take leave during the final month of pregnancy and during the first three months postpartum.

Workers in the U.S., however, get only a chance at unpaid leave for three months after birth of a child. And that narrow benefit, part of the 1993 Family and Medical Leave Act (FMLA), applies only to private companies with more than 50 employees (the unpaid offering also applies to public employees). Almost half of the U.S. population is ineligible. And because there are no federal paid-leave requirements, only about one in eight private-sector employees has a paid option. (*Scientific American* gives 10 days.)

That needs to change to improve our health and economy. Paid leave will keep families healthier. In countries with such policies, it has reduced infant mortality by as much as 10 percent. It also helps to improve new parents' emotional well-being. And multiple studies indicate that paid maternity leave is associated with increased rate and duration of breast-feeding. That practice, pediatricians agree, promotes better health for a newborn.

Paid leave need not come at the expense of profits, either. During this year's presidential campaign, Donald Trump cited concerns about businesses' bottom line for his reluctance to embrace the paid approach (although ultimately he did propose a six-week paid-leave plan). There is already good evidence that paid leave would not hurt businesses. The experience of a few states that have enacted paid-leave laws shows they produce good results for employers and employees alike. California, Rhode Island and New Jersey all have mandatory paid-leave requirements, ranging from four to six weeks at partial pay. The money comes entirely from employee payroll deductions—not out of employers' pockets. In studies of those states, most businesses subsequently reported that such policies had no negative effect on their profitability or productivity, and employers said employee morale improved. Private companies in the U.S., including Microsoft, Goldman Sachs, Nestlé and Facebook, think it makes good economic sense, too. They say they voluntarily offer their employees paid family leave to increase workplace competitiveness and employee retention.

Scattered state and company support for paid leave, however, is not enough. A national policy would enable employees and companies throughout the country to share in these documented advantages. It would also help eradicate other workforce inequities, including long-standing gender pay gaps that are exacerbated when women exit their job to tend to children. (Paid leave allows women to remain in the workforce, reducing holes in a résumé, which helps to address the differences.) If more people are working, that may also reduce government spending on public assistance.

Such policies also promote shared responsibilities in the household. One study of working fathers in the U.S. found that new fathers who took leave of two weeks or more were much more likely to be involved in their child's care nine months after birth—including feeding, changing diapers and getting up during the night when their child needed a parent.

Now, with a new chief executive and Congress, is the time to take federal action and secure at least a month of paid family leave before ultimately scaling up to several months of paid support. Without paid family leave, we are all paying too steep a price. SA

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Hannah A. Valantine is the first chief officer for scientific workforce diversity at the National Institutes of Health.

Science Has a Gender Problem

Women face discrimination of many kinds. We need a culture change

By Hannah A. Valantine

Are women scientists getting an even shake as they try to advance their careers? Research on the subject suggests maybe not. For example, a new study published in the journal *Academic Medicine* finds that a substantial salary gap favors male scientists to the tune of $20,000. Another study suggests evidence of bias against women's ability to keep a steady stream of research funding, which is the lifeblood of any scientist's career.

By some measures, female scientists are doing well. Women make up about half of all new Ph.D.s and M.D.s., and roughly equal numbers of women and men start as assistant professors. Moreover, research has shown that white women were as likely as white men to earn a research project grant from the National Institutes of Health, a crucial first step toward achieving career independence and tenure. That same study, however, showed that Asian and African-American women scientists were less likely to receive funding, pointing to a "double bind" for women of color. Such nuances matter in a hypercompetitive research-funding environment in which only one in three scientists (women or men) gets enough NIH grant money to keep a laboratory afloat.

And there are many more nuances. For example, after getting research money, women may face hurdles to keeping funds flowing long enough to make discoveries. After three to four years of a research grant, scientists must convince the NIH that they have gotten results to continue receiving money for more research. In a text-mining analysis of comments used by "peer" scientists to review grants, researchers discovered that those reviewers used more laudatory words such as "outstanding" and "excellent" to describe women's applications yet scored them lower than submissions by men. This evidence suggests that reviewers use different standards to judge applications from women.

Women also receive less funding from universities right from the beginning of their careers: on average, they get 40 percent less money to start their labs. Time off from the job is often treated differently as well. Men often use "culturally acceptable" paid leave, such as sabbaticals, which have no impact on their pay. Although women also take sabbaticals, they are more likely than men to take family-related leave, which still incurs stigma. In many cases, women simply choose not to take leave. We need to revisit outmoded, family-unfriendly policies. We should also reexamine academic biases against part-time faculty and reframe work-life issues as career-advancing rather than career-pausing. We know that flexible work arrangements can improve satisfaction and even performance.

We can fix at least one issue—compensation—simply by holding university deans and presidents accountable. Salary equity should be a critical element of leadership performance reviews. In the case of grants, we know one group that is disadvantaged. A recent NIH analysis showed that applications from African-American scientists are funded at a significantly lower rate than applications from white scientists (11 versus 17 percent). The NIH is now studying whether removing all personal identifiers in a grant application makes a difference in how it is scored. If it does, then removing personal identifiers may also affect how women's applications are reviewed. Finally, we must address the recently highlighted problem of sexual harassment, which affects both genders but which is disproportionately suffered by women.

Women bring unique perspectives to research, and as a nation, we need all the best ideas we can get. It is in everyone's interest to correct this issue, and progress relies on women and men shifting culture. Transgressions are often unintended. But the stereotypes we carry unconsciously, and often unintentionally, lead to biases, which have powerful effects on satisfaction, productivity and career advancement. Our failure to eliminate the inequities facing women in science would represent a failure for women and men alike, as well as for the enterprise of biomedical research. SA

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Illustration by Vidhya Nagarajan

ADVANCES

"The stars are the landmarks of the universe."
—*John Herschel* (1792–1871)

INSIDE

- A second sighting of water plumes on Europa
- A high-voltage lab
- The teenager who won big for a homemade polymer
- Why sulfur is so smelly

ASTRONOMY

The Milky Way, Transformed

A new map of our galaxy will improve understanding of stellar physics—and ultimately of the Milky Way's entire history

Astronomers are about to unfold a new map of cosmic reality. The Gaia spacecraft, launched in late 2013 by the European Space Agency, is on a five-year mission to chart the heavens in unprecedented detail—and the first set of coordinates has been released. By the end of Gaia's run, it will have pinpointed the positions of approximately one billion stars in the Milky Way and nearby galaxies with a resolution so high it can spot objects as small as five microarcseconds—roughly half the size of a dime sitting on the moon as seen from Earth. Its billion-pixel camera will also record each star's distance and two-dimensional velocity, providing a fresh understanding of our galactic neighborhood.

To Kathryn Johnston, an astronomer at Columbia University, creating this star chart is analogous to mapping Earth's continents for the first time—transforming an image of a vague green and blue blob into a world with mountains, rivers and valleys. "In a strange way, we almost don't know what our galaxy looks like as accurately as we know other galaxies," Johnston says, explaining that it seems nearly impossible to take a picture of a whole galaxy when you are stuck inside of it. But that is exactly what Gaia will do.

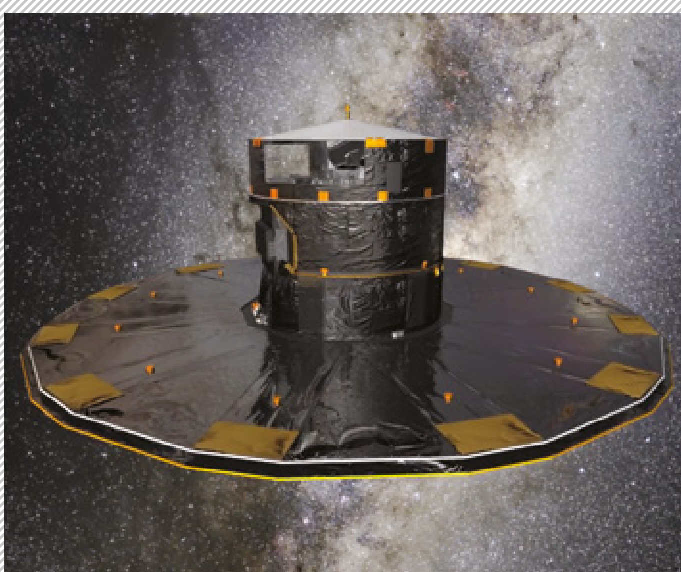
The updated map has been highly anticipated; on the first day of the initial data release in September at least 10,000 people accessed the archive, says Gaia project scientist Timo Prusti. The dataset includes the preliminary positions of one billion stars (future data releases will improve these numbers) and the distances and sideways motions of the two million brightest stars in the sky. With each subsequent release, the distances and motions of stars at greater and greater distances within the galaxy will be revealed, creating successive maps that radiate outward from the sun like ripples on a pond.

Findings are already pouring in. For instance, Gaia scientists have used the preliminary results to resolve a controversy over the distance to the Pleiades star cluster—the famous "Seven Sisters." The debate, which was sparked by the final data release from Gaia's precursor, the Hipparcos mission, was far from trivial: without a correct distance, astronomers could not determine the stars' luminosities or radii with any certainty. A precise measurement (Hipparcos' was wrong) is also important because the Pleiades embody a benchmark cluster for understanding how stars form. "The theory for young stars is quite tricky," Prusti says. "Because they're unstable, there are many alternatives. So one really needs to have precise observations to constrain these models."

Other research groups are using the new data to investigate unusual stars (those that appear excessively faint or bright or are moving too rapidly or sluggishly). "Astronomers think we understand how stars work pretty well," says David Spergel, an astronomer at Princeton University. "But I suspect that when our data get better we'll discover that while we have the basic picture right, there are things we thought we understood that we don't." Planetary physics is also involved as astronomers search for stars that host interesting planets. Although Gaia has not yet discovered any such worlds, scientists hope the spacecraft will ultimately detect thousands or even tens of thousands.

Despite the September bounty, astronomers are still eagerly awaiting Gaia's next observations (there will be four more releases). "Although there is lots of science we can do with the first data release, it's nothing like the science we're going to be able to do at the end of the mission," says David Hogg, an astronomer at New York University. With the full dataset in 2022, researchers will be able to tackle the mission's main scientific goal: to unravel the structure and dynamics of the Milky Way and to illuminate its violent history. For instance, some of the Milky Way's stars were born within smaller galaxies, which were later cannibalized by our monstrous galaxy. Today the remnants of those puny galaxies can be seen in the form of faint streams of stars that stretch across the sky, providing clues about the timeline of our neighborhood's evolution. "You're finding galaxies that were alive in the past, you're finding the orbits that they were on and you're finding the stars associated with them. So you can build up the history of our galaxy eating other galaxies," says Columbia's Johnston.

Ultimately Gaia's full legacy is impossible to pin down in advance. On top of its main mission, the satellite will also observe thousands of nonstar objects in the solar system, possibly map the distribution of dark matter in the Milky Way, and chart the positions of hundreds of thousands of quasars—the blazing cores of ancient galaxies. In the long term, Gaia will also improve observations from other telescopes because the instruments will know exactly where to look, Prusti says. In the meantime, Hogg has organized "Gaia Sprints" in New York City and Heidelberg for all types of astronomers to come together and explore the data in a collaborative environment. "I think that the right way to think about it—and the real reason everyone is excited—is that it's an opportunity for discovery," Hogg says. "People are excited because it's a new world. And the first data release is just a teaser for that new world." *—Shannon Hall, with additional reporting by Sara Goudarzi*



BY THE NUMBERS

1.5 million kilometers
The Gaia spacecraft's distance from Earth

50x higher
Resolution of Gaia's camera compared with the one onboard the Hubble Space Telescope

30x more
Amount of light Gaia's primary mirrors can collect compared with the star-mapping satellite Hipparcos

70
Number of times Gaia will observe each of its one billion targets

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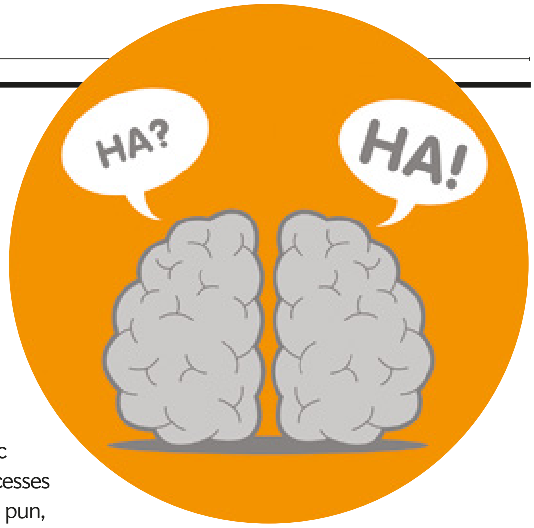
NEUROSCIENCE

Your Pun-Divided Attention

Left and right brain hemispheres have different functions when processing humor, teaming up to form the ultimate comedy duo



Puns are divisive in comedy. Critics groan that they are the "lowest form of wit," a quote attributed to various writers. Others—including Shakespeare—pun with abandon. The brain itself seems divided over puns, according to a recent study published in *Laterality: Asymmetries of Body, Brain and Cognition*. The results suggest the left and right hemispheres play different roles in processing puns, ultimately requiring communication between them for the joke to land.

To observe how the brain handles this type of humor, researchers at the University of Windsor in Ontario presented study participants with a word relating to a pun in either the left or right visual field (which corresponds to the right or left brain hemisphere, respectively). They then analyzed a subject's reaction time in each situation to determine which hemisphere was dominant. "The left hemisphere is the linguistic hemisphere, so it's the one that processes most of the language aspects of the pun, with the right hemisphere kicking in a bit later" to reveal the word's dual meanings, explains Lori Buchanan, a psychology professor and co-author of the study.

This interaction enables us to "get" the joke because puns, as a form of word play, complete humor's basic formula: expectation plus incongruity equals laughter. In puns—where words have multiple, ambiguous meanings—the sentence context primes us to interpret a word in a specific way, an operation that occurs in the left hemisphere. Humor emerges when the right hemisphere subsequently clues us in to the word's other, unanticipated meaning, triggering what Buchanan calls a "surprise reinterpretation."

The study jibes with previous observations that brain injuries to the right hemisphere can be associated with humor deficits in some people, who understand a joke's meaning but "don't think things are funny anymore," Buchanan says. She hopes this and future studies may lead to rehabilitative training to help such individuals get back their sense of humor. Bottom line: puns get on everyone's nerves. —*Roni Jacobson*

BIOLOGY

Organelle Overhaul

A cell's lysosomes are responsible for much more than trash collection

The lysosome was once thought of as the trash can of the cell, a dead-end destination where cellular debris was sent for disposal. But a growing body of research shows that this enzyme-filled vesicle is more active than it originally appeared to be—with some scientists now calling it a control center for cellular metabolism, the set of chemical reactions within a cell that keep it alive and well. Discoveries over the past decade "have elevated the lysosome to a decision-making center involved in the control of cellular growth and survival," according to Roberto Zoncu, a cell biologist at the University of California, Berkeley. His review of the organelle's changing reputation was published in September's *Journal of Cell Biology.*

As most high schoolers learn, the lysosome carries out waste disposal and recycling. In a process known as autophagy (meaning "self-eating"), it takes in old cellular components and unneeded large molecules, such as proteins, nucleic acids and sugars, and digests them with the help of enzymes and acids. The cell can then use these broken-down pieces as fuel or as building blocks for new molecules. Understanding this process is so important that Yoshinori Ohsumi won the Nobel Prize in Physiology or Medicine in October for his autophagy work in the 1990s. Yet that's not all the organelle can do, it seems.

For instance, one developing line of research indicates that the lysosome can sense how well nourished a cell (and thus an organism) is. When an organism is fasting or starving, the organelle prompts the cell to create more lysosomes containing enzymes that can digest fat reserves—a source of energy. Conversely, when the organism is well fed, lysosomes send out a message to the cell that resources are available to spend on growth or reproduction. Essentially the lysosome acts as a master switch in the cell to toggle between breaking things down or building them up, says Andrea Ballabio, a geneticist at the Telethon Institute of Genetics and Medicine in Italy who studies the lysosome's role in health. Because of the organelle's ability to control fat metabolism, University of Virginia biologist Eyleen O'Rourke predicts that lysosomes could someday serve as therapeutic targets for metabolic diseases such as obesity.

The reigning image of the lysosome is changing outside of metabolism as well. It also seems to be involved in life span and longevity; studies have shown that when lysosomes do not function properly, an organism does not live as long—perhaps because cellular debris and other waste build up. Some scientists are also starting to think that lysosomes may be culprits in neurodegenerative illnesses, following studies from researchers at New York University who have shown that a defect in a lysosomal gene accelerates Alzheimer's disease. What all this research makes clear is that lysosomes should no longer be considered a dead end. Instead they might just be the way forward for a new generation of lifesaving drugs.

—Monique Brouillette

ANIMAL BEHAVIOR

The Brainy Big Cats

New experiments with lions suggest sociality in animals promotes high-level cognition

KOBUS SCHOEMAN *Getty Images*

An African lion gazes up at a suspended wood box. Inside is a hunk of raw beef. To enjoy the snack, the lion needs to yank on a rope descending from the box, which is attached to a spring-loaded door latch. The scheme: to test the charismatic cat's cognitive abilities.

The social intelligence hypothesis posits that having to navigate a complex communal life, which involves challenges such as keeping track of who is a friend and who is an enemy, has pushed group-living animals to evolve the mental machinery required to solve and remember mental tasks such as the box puzzle. In other words, social complexity leads to cognitive complexity.

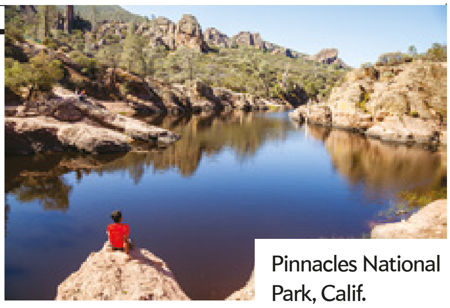
Researchers have long explored this idea by observing animals such as chimpanzees, dolphins and elephants, but biologist Natalia Borrego of South Africa's University of KwaZulu-Natal focuses on big cats. "You have a lot of closely related species with these diverse ecological challenges and different social systems," she says.

Borrego and her team presented the rope challenge to 12 captive lions at Florida's Lion Country Safari. Eleven of them successfully solved it: seven on their own and four after watching another lion do it. Ten of the 11 recalled the solution five to seven months later. The results were recently published in the journal *Animal Cognition.*

"That they remember what they've learned isn't terribly surprising," says Oakland University cognitive psychologist Jennifer Vonk, who studies cognition in bears. But she finds the social facilitation—the fact that some individuals figured it out after being paired with another lion—particularly exciting. "We don't always see those kinds of effects—even in primates," she adds.

In a follow-up experiment using a similar conceptual puzzle, lions outperformed leopards and tigers (which are both solitary big cats)—more evidence for the social intelligence hypothesis. But Borrego acknowledges that habitat and diet could also be factors in cognitive evolution. "The evolution of cognitive complexity is itself complex," she says.

—Jason G. Goldman



Pinnacles National Park, Calif.

ENVIRONMENT

Obama's Conservation Legacy

President Barack Obama has called conservation "a cornerstone of my presidency"—and the numbers back him up. He has protected more American land and water than any of his predecessors, in part thanks to the Antiquities Act passed by President Theodore Roosevelt in 1906. The act gives the executive branch the relatively unrestrained power to protect land by proclamation, without having to go through Congress. The Obama administration has also overseen the removal of more recovering animals and plants from the endangered species list than all previous administrations combined. "We believe the president is going to leave a significant conservation legacy through his leadership," says Dan Chu, director of the Sierra Club's Our Wild America campaign.

—Ryan F. Mandelbaum

BY THE NUMBERS

360,000 square miles
Land federally protected by Theodore Roosevelt

6,250 square miles
Land federally protected by Barack Obama

856,000 square miles
Marine ecosystems federally protected by Barack Obama

22
New properties added to the National Park System under Obama

19
Endangered species delisted during Obama's time in office

AMIT BASU Getty Images (Pinnacles National Park); SOURCES FOR STATISTICS: NATIONAL PARK SERVICE (Roosevelt-protected land and new parks); U.S. DEPARTMENT OF THE INTERIOR (Obama-protected land and water); U.S. FISH & WILDLIFE SERVICE (endangered species delisted)

SPACE

Hope Springs Eternal for Easy Access to Water on Europa

Water vapor erupting from Jupiter's moon could offer new pathways for exploring its subsurface ocean

COURTESY OF NASA, ESA AND KURT RETHERFORD *Southwest Research Institute*

An ocean within Jupiter's icy moon Europa may be intermittently venting plumes of water vapor into outer space, according to a new study in the *Astrophysical Journal.* The finding suggests the ocean, thought to lie underneath perhaps 100 kilometers of ice, may be more amenable to life—and more accessible to curious astrobiologists—than previously thought. "If there are plumes emerging from Europa, it is significant because it means we may be able to explore that ocean for organic chemistry or even signs of life without having to drill through unknown miles of ice," says study lead William Sparks, an astronomer at the Space Telescope Science Institute. The plumes would also suggest a potent source of heat lurking within Europa that could sustain living things.

With the help of the Hubble Space Telescope's imaging spectrograph, Sparks and his team observed Europa 10 times between late 2013 and early 2015 as it crossed the face of Jupiter. Watching in ultraviolet light, in which Europa's icy surface appears dark, they looked for silhouettes of any plumes contrasted against Jupiter's bright, smooth cloudscapes. Intensive image processing unveiled what looked like three instances of ultraviolet shadows soaring over the southern edge of Europa's dark bulk. If the shadows were produced by plumes and not glitches in Hubble's instruments, they would collectively contain an estimated few million kilograms of water and reach about 200 kilometers above Europa's surface.

Sparks acknowledges that his team's results remain frustratingly hazy. "These observations are at the limit of what Hubble can do," he says. "We do not claim to have proven the existence of plumes but rather to have contributed evidence that such activity may be present." Previous evidence of similar plumes was reported in 2014 in *Science,* but after follow-up observations, those water vapor spouts seemed to have stopped—or were not there in the first place. In that regard, "this [new observation] is exactly as likely as the last detections" to be real, says Britney Schmidt, who is a planetary scientist at the Georgia Institute of Technology and was not involved with the research.

Such caution is justified—the presence (or absence) of Europa's plumes could profoundly alter the future of interplanetary exploration, redirecting billions of dollars in funding toward new exploratory missions. NASA and the European Space Agency already aim to lead missions to the tantalizing Jovian moon in the 2020s. *—Lee Billings*

1

Holbøll with a high-voltage sphere gap (*1*). A 400,000-volt single-phase transformer (*2*).

WORKPLACE

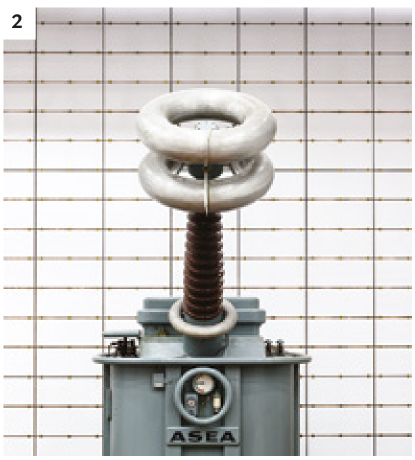
Surge Protector

A high-voltage lab in Denmark explores how to safeguard wind turbines from lightning

Wind turbines are lightning magnets—and strikes on these tall, spinning structures can cause significant damage. Blades explode; generators and control system electronics fry. To figure out how to safely disperse lightning, turbine manufacturers have turned to the Technical University of Denmark's High Voltage Lab. Using giant versions of standard electrical devices such as sphere gaps, transformers and capacitors, the facility can generate huge arcs of electricity—up to 800,000 volts AC. The equipment helps companies test how new turbine parts or mechanisms will respond to electrical surges out in the field.

"Many high-voltage labs, they look like something from the 1960s," says Joachim Holbøll, a professor and deputy head of the university's Center for Electric Power and Energy. "But we are doing necessary stuff in there with the newest equipment. Parts of this will always look a little old-fashioned, but that is simply because it works."

2



The lab is also tackling a new problem: wind turbines are getting so tall that they frequently generate "up lightning." This type originates from the turbine's own electric field and leaps from the tip of a blade to meet a downward bolt. The direction of the bolt does not change the form of protections that the turbines need, Holbøll says. But understanding these dynamics is critical to modeling the frequency of lightning strikes at wind farms, and the High Voltage Lab is working to verify theoretical and computational descriptions of this phenomenon. In 2015 wind power provided 42 percent of the electricity Denmark consumed. *—Karl J. P. Smith*

ALASTAIR PHILIP WIPER

IN THE NEWS

Quick Hits

FRANCE

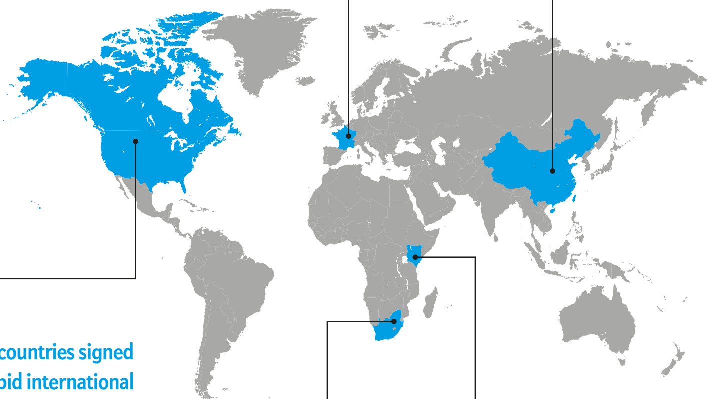
A new law bans all plastic kitchenware, requiring that alternatives be compostable. It follows on the heels of a similar national law that prohibits plastic bags in supermarket produce sections, taking effect in January.

CHINA

An announcement from Chinese officials seemed to confirm that the country's space agency had lost control of its Tiangong-1 space station, which has been in low-Earth orbit since 2011 and was last occupied in 2013. The 8.5-metric-ton spacecraft will most likely fall to Earth in late 2017; experts predict it will largely burn up on reentering the atmosphere.

U.S. AND CANADA

The number of breeding North American birds has plummeted by approximately 1.5 billion over the past 40 years, according to a new report. Forty-six species have lost at least half their populations—primarily through urbanization and habitat degradation.



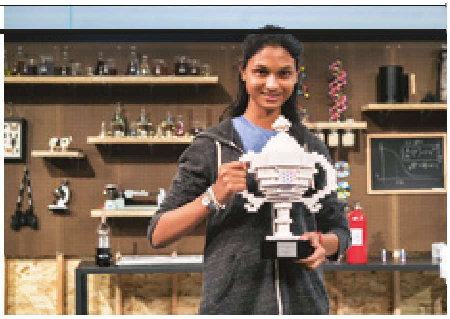
SOUTH AFRICA

Representatives from more than 100 countries signed an agreement in Johannesburg to forbid international trade in pangolins. The armored mammal's scales are used in traditional Chinese remedies, and researchers estimate that at least one million have been illegally traded since 2000 despite previous scattershot laws.

KENYA

The Kenyan government is set to deliver 1.2 million laptops to the country's 23,000 primary schools by the end of this year—an effort to prepare students to be competitive in Kenya's emerging economy, in which officials hope technology will play a large part.

For more details, visit
www.ScientificAmerican.com/dec2016/advances



COURTESY OF ANDREW WEEKS

EDUCATION

Teen Takes on Drought

A polymer that could keep crops hydrated places first at the Google Science Fair

Kiara Nirghin was leafing through a newspaper one day when she noticed several stories about farmers struggling with drought. Nirghin, a high school junior in Johannesburg, had known South Africa was in the midst of an intense drought, but in that moment she realized the problem extended far beyond her country: "It's affecting the whole world. And to this point, there hasn't been something that has revolutionized drought."

Nirghin set about brainstorming on how to ensure that crops have access to water—even during the most severe stretches of dry weather. Her simple solution earned her the grand prize at the Google Science Fair in September. (*Scientific American* co-sponsors the awards.)

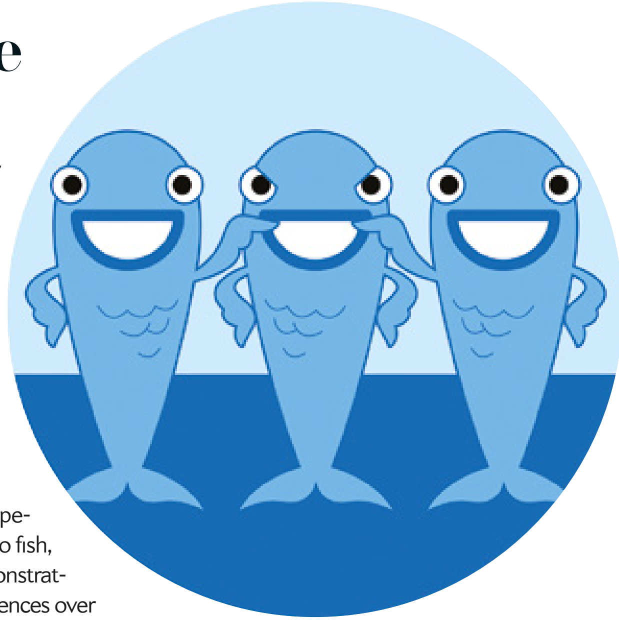
For her project, Nirghin created a biodegradable and superabsorbent material that can be "planted" alongside crops to create "mini reservoirs of water in the soil," she explained in her presentation. First she boiled orange peels in water to produce a liquid rich in pectin, a highly absorbent carbohydrate. Then she combined the pectin with pieces of dried orange peels and avocado skins, baked the mixture to remove moisture and crushed it all into a powder. Finally, she mixed the powder with more peels and skins. The resulting polymer could hold 300 times its weight in water. In tests, the invention kept soil moist—and plants grown with it were taller and healthier and produced more flowers.

Nirghin hopes her material will help drought-stricken communities improve their food security. "Nirghin's project was inspiring for the judges," says Mariette DiChristina, *Scientific American* editor in chief and chief judge of the Google fair since its inception in 2011. "They were impressed with her excellence of method, the project's capacity for impact and her passion for improving the world through science." —*Catherine Caruso*

ANIMAL BEHAVIOR

One's True Nature

An animal's personality may bend to conform to group dynamics, but it ultimately remains constant



As any pet owner will tell you, humans aren't the only animals with personalities. And it isn't just dogs and cats. In recent years scientists have found that members of many species, from hermit crabs to rats to fish, have unique dispositions, demonstrating consistent behavioral differences over time and across varying situations.

But how do social situations affect individual personalities? University of Bristol biologist Christos C. Ioannou and his colleagues sought to find out by turning to a small fish called the three-spined stickleback, which inhabits brackish coastal waters throughout the Northern Hemisphere. "They're found both as individuals and in social groups in the wild," making them perfect for personality assessments across different settings, Ioannou says.

The researchers took 80 fish and placed each under a protective cover at one end of a tank. At the opposite end was some food. Crossing the tank to feed would seem risky to the sticklebacks because open water typically exposes them to the threat of predation.

Each fish behaved consistently over several days. Bolder ones quickly left the safety of the refuge to go for the food. Timid ones took longer to emerge and swam across the tank more cautiously. But when 10 sticklebacks were placed under the cover together, each fish's individual persona faded away. As with humans, the bolder individuals served as group leaders—albeit careful ones. "The first individuals come out relatively quickly, but it almost looks like they realize they're not being followed and so wait for others to catch up with them," Ioannou says. When separated from the group later on, the fish regained their original personalities. The results were published in September in *Science Advances.*

When 10 sticklebacks were placed under the cover together, each fish's individual persona faded away.

The new findings suggest that group dynamics tamp down individual personalities, and the researchers say it is the first time that such suppression has been explicitly linked to an underlying cause: the need to conform when faced with a risky decision.

Animal personality researchers have historically focused on individuals while ignoring the way they behave in groups, and collective behavior researchers have focused on groups while downplaying individual differences, according to University of St. Andrews animal behavior researcher Mike Webster, who was not involved in the work. "What this study really does is bring those two streams of research together," showing that animal personalities are flexible yet also persistent, he says. *—Jason G. Goldman*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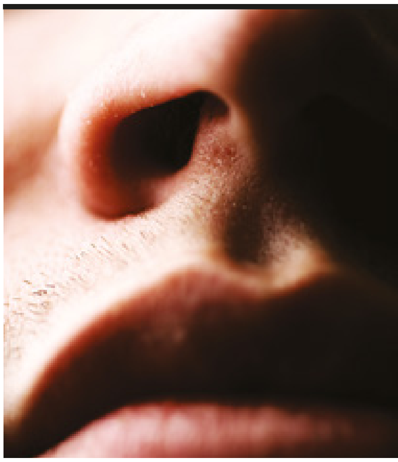


DUNCAN WALKER *Getty Images*

OLFACTION

P.U. to Cu

Copper enhances smelly sulfur odors in the nose

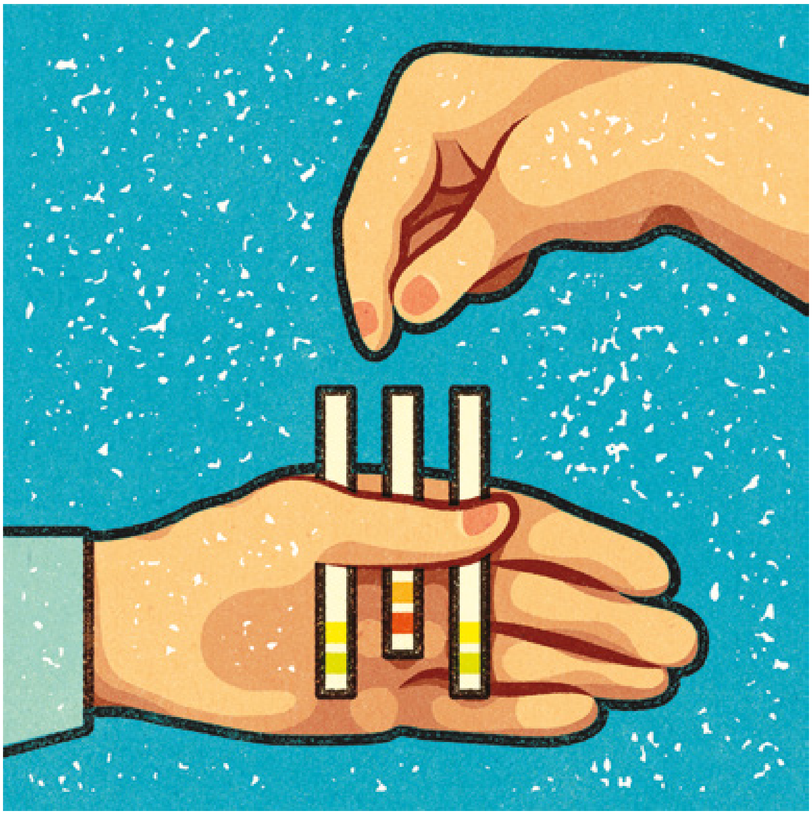
Gas leaks, garlic breath, skunks in the neighborhood—ah, the scent of thiols. The human nose is particularly sensitive to these sulfur-containing compounds, which is no surprise given that they are often associated with things to avoid. But how exactly are our nostrils (and those of other mammals) so adept at sniffing out thiols when other odors, such as bleach or vinegar, require higher thresholds of molecules in the air for us to detect them?

The hypersensitivity comes down to the metal copper, according to a team of chemists from the U.S. and China. As they reported this fall in the *Journal of the American Chemical Society,* the researchers discovered that the same receptors in the nose that pick up these unpleasant-smelling molecules also bind with particles of copper that reside in nasal mucus. The metallic partner amplifies a thiol's intensity by up to 1,000 times. And in experiments in which the scientists created thiol receptors that could not bind with copper, sensitivity to the odorant all but disappeared.

Evolutionarily, it pays to have a nose that can pick up the minutest presence of thiols, says study co-author Eric Block, a chemist at the University at Albany, State University of New York. The sulfur compounds are released by rotting food, for instance, and some predators give off olfactory cues to their presence in this form.

This is the first time a metal has been implicated in smell, and the study will likely encourage other scientists seeking to better understand olfaction to look for metallic sidekicks, says Robert Crabtree, a chemist at Yale University. Crabtree first speculated about copper's role in thiol olfaction in 1977. —*Mark Anderson*

Charles Schmidt is a freelance journalist based in Portland, Me., covering global health and the environment.



When Medical Tests Mislead

The FDA cracks down on lab tests that are often technically accurate but nonetheless harmful to human health

By Charles Schmidt

Every year in the U.S., doctor's offices and hospitals order billions of laboratory tests to measure everything from cholesterol levels in the blood to the presence of a gene thought to increase the risk of developing Alzheimer's disease. Physicians and patients typically assume that they can trust the results of these tests. And most of the time they can. But not all lab tests are equally reliable, and faulty ones can have serious consequences. Sometimes they fail to detect life-threatening conditions. Other times they indicate a problem that does not exist, which can lead to unneeded, perhaps even dangerous treatments.

Through a quirk of regulatory history, many such tests are not subject to the same medical standards as other tools used to identify risk for disease or to definitively diagnose a condition. These are called lab-developed tests, or LDTs, defined as tests that are manufactured and interpreted by the same individual lab that designed them—in contrast to, say, a quick strep test meant to be used and understood by a wide variety of personnel in doctor's offices everywhere. Most people first encounter an LDT during a checkup when the physician is faced with a diagnostic dilemma that cannot be resolved by widely available blood tests.

The trouble is, experts believe many of these tests are not useful, and some may even cause harm by convincing too many people that they have a rare illness when they do not, diagnosing them with a condition that has so far not been shown to be harmful or reassuring them that they are healthy when in fact there is no scientifically credible way to know if that is indeed the case. "We tend to think of lab tests as being the ultimate truth," says Ramy Arnaout, an assistant professor of pathology at Harvard Medical School. "But no test is 100 percent accurate, and some of these LDTs aren't medically useful at all."

The U.S. Food and Drug Administration is now taking steps to restore confidence in the reliability of lab-developed tests. In 2014 the agency released proposed guidelines that will subject the measures, for the first time, to federal oversight—including having to submit evidence of efficacy to it before the tests may be marketed. Although the FDA would not comment for this story, several industry sources believe the final rulings may begin taking effect soon, much to the chagrin of some lab directors who say that the requirements could boost costs and hinder medical practice.

WIDENING LOOPHOLE

TWENTY-FIVE YEARS AGO LDTs played too small a role in medical practice for the FDA to pay them much attention. Only a few—most notably Pap smears for the detection of cervical cancer—were widely used. FDA officials adopted a policy of "enforcement discretion," which meant they pretty much left LDTs alone while they focused on tools with an apparently greater potential for harm, such as malfunctioning pacemakers.

After researchers developed new genetic engineering techniques in the 1990s, however, the possibilities for LDTs expanded dramatically. Whereas previous generations of LDTs looked for a handful of unusual proteins, for example, some of the newly emerging genetic tests could sort through any number of the three billion base pairs, or letters, of the DNA alphabet found in the human genome, looking for abnormalities related to disease. In addition, testing became automated, making LDTs increasingly easier to design and use.

Illustration by Alexei Vella

The improved technology led to an enormous rise in the number and variety of LDTs that came to market. By some estimates, about 11,000 labs now offer between 60,000 and 100,000 of them; no one knows precisely how many because, of course, these tests do not have to be registered anywhere.

Under current federal regulations, LDTs enjoy a big loophole, which means they do not have to be evaluated for their medical usefulness. Nor are they required to have research about them made public. The lab that created them does need to meet certain fundamental standards of scientific practice. But the FDA does not vet the tests either before or after doctors can start ordering them for patients, as it does for most prescription drugs or medical devices.

This loophole means that companies ranging from small start-ups offering just one or two tests to much larger diagnostic labs that offer thousands of tests can develop and charge for new LDTs much more easily than they can for most other categories of medical products. With the rise in the number of tests has come a series of reports showing that certain ones have already hurt people by delivering misleading results.

CLINICAL VALIDITY

THE FDA HAS CITED 20 different types of LDTs as especially troubling, including Lyme disease and whooping cough tests that regularly give wrong answers and LDTs that purport to determine a woman's risk for ovarian cancer such as by measuring the presence of the protein CA 125 in the blood. In September the agency concluded that screening measures for this protein offered "no proven benefit" and warned physicians against recommending or using them.

Many of the tests that have raised the FDA's ire may indeed measure what they claim to measure. The problem is that the measured substance may not be a good indicator of a specific medical problem. In the case of the ovarian cancer tests, for instance, high levels of CA 125, which is made in the ovaries, should in theory signify the presence of extra ovarian cells—in other words, the presence of a tumor. In reality, it turns out that many women with high levels of CA 125 do not have ovarian cancer, and, conversely, many women with cancer do not have high levels of CA 125. Thus, measures of CA 125 cannot be trusted to give an accurate diagnosis of cancer—and yet a number of women who tested positive apparently feared the possibility of cancer so much that they decided to have their healthy ovaries removed anyway.

One way that investigators determine whether a medical test should be used as a guide to a patient's condition is by applying a somewhat obscure statistical ratio called a positive predictive value, or PPV. This measure takes into account just how common a condition might be in a given group of people.

Why such a consideration would be important in determining a test's usefulness may be best understood by analogy. If you drop a baited hook into a barrel full of fish, the chances that a tug on the line means that you have caught a fish are pretty high. On the other hand, dropping the same baited hook into a freshwater lake that has not been stocked with fish makes it much less likely that any given tug on the line represents a fish, as opposed to, say, a tree snag. Because the barrel contains many more fish for a given volume of water than the lake does, a tug in the container has a PPV close to 100 percent, whereas that of a tug in an unstocked lake is much less than 100 percent.

This crucial statistical distinction explains the problem the FDA has with one current ovarian screening test, which its developer claimed had a PPV of 99.3 percent. Closer analysis by independent biostatisticians revealed, however, that the value was calculated on the basis of a single experiment in which half the patients were already known to have ovarian cancer—a highly selected group that is the medical equivalent of a stocked pond.

When the researchers recalculated the PPV using ovarian cancer's true frequency in the general U.S. population of one case for every 2,500 postmenopausal women, the PPV plummeted to just 6.5 percent. In other words, only one in every 15 patients who received a positive result from this malignancy test would have actually had ovarian cancer. The other 14 would, if they had relied on this test alone, very likely have undergone unnecessary operations to remove their otherwise healthy ovaries because they would have mistakenly believed they had a 99.3 percent chance of having cancer.

CHANGING FOCUS

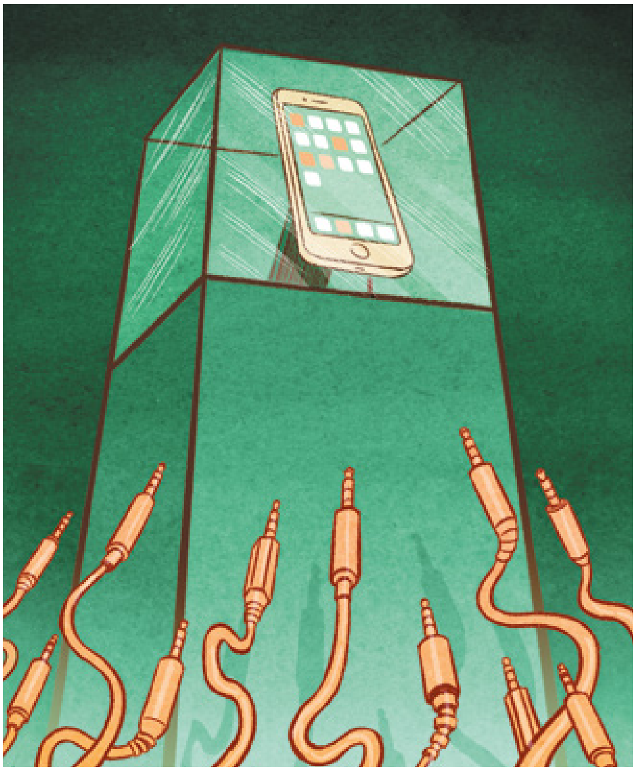
BECAUSE THE FDA does not have the resources to oversee all the LDTs that have come to market in recent years, the agency plans to divide them into three categories, based on the likelihood that a misleading or incorrect result from a particular test could cause substantial harm. Under the new guidelines, LDTs would be considered high risk if inaccurate results could lead to death or prolonged disabilities. Such tests would come under the greatest inspection, information about them would need to be entered in a national database, and manufacturers would have to prove their safety and efficacy to the FDA before they could be sold. "Basically, the FDA wants to see the supporting evidence before it allows a high-risk LDT to go out on the market," says Joshua Sharfstein, a physician and professor at the Johns Hopkins Bloomberg School of Public Health.

Even this targeted approach worries many industry leaders and some professional medical societies, including the American Medical Association. "It really depends on how the FDA chooses to define high risk, and that currently isn't clear," says Curtis Hanson, chief medical officer at Mayo Medical Laboratories in Rochester, Minn., which conducts 25 million lab tests a year. "High-risk tests could amount to between 1 and 10 percent of LDTs on the market today. How is the FDA going to review and find the rare cases where you have problems and do that in an efficient way that doesn't slow progress?"

For patients and their physicians, the question is much more basic. Why should they ever have to wonder whether a commercially available medical test does more harm than good? SA

SCIENTIFIC AMERICAN ONLINE Read the FDA's report on 20 particularly troubling lab tests at ScientificAmerican.com/dec2016/fda-oversight

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



Resistance Is Futile

Apple has dropped the headphone jack—and soon everyone else will, too

By David Pogue

This past September, Apple released new iPhone models without headphone jacks. The people were not pleased.

"It's eliminating a connector and adding inconvenience in the name of profit," one commenter wrote. "Apple wants to see just how stupid the public really is," said another. "There is absolutely no reason to get rid of a perfectly working universal headphone jack," added a third.

As it turns out, there *is* a reason. The plug itself is small. But the corresponding receptacle on the *inside* of the phone is relatively enormous. By removing it, Apple says, it was able to fit in a bigger battery, giving the iPhone 7 two more hours of life per charge, a stabilized camera for fewer blurry photographs and stereo speakers.

Apple includes, in the box, both a new pair of earbuds (they plug into the phone's charging jack) and a two-inch adapter for existing headphones. But those wired approaches are meant to be stopgap measures until we all buy *wireless* headphones, which now cost as little as $17. (This year Bluetooth headphones overtook sales of wired ones for the first time.) Everything else is going wireless, Apple says, so why not our audio?

If you were an observer from Alpha Centauri, therefore, you might wonder what all the hullabaloo is about. Apple killed off a component popularized 52 years ago, offers two free ways to replace it and exploits the interior space with better features. What's the big deal?

If you were a human observer for the past 20 years, on the other hand, you might wonder about our short memory.

Apple's inclination to kill off "standard" components in the name of progress is no surprise. This, after all, was the company that famously eliminated floppy drives, CD-ROM drives and dial-up modems. And it got rid of physical keyboards on smartphones. It has discontinued a series of its own connectors, such as ADB, SCSI, FireWire and the original iPhone charging jack.

And every single time, the public is outraged. "The iMac is clean, elegant, floppy-free—and doomed," went the *Boston Globe*'s 1998 review. (The iMac quickly became the best-selling computer in the U.S.) But every single time, the computer industry's reaction is also the same: to follow suit. Dell, Hewlett-Packard and other companies dumped the floppy drives and dial-up modems from their standard PCs, too.

So the pattern is now clear: The tech companies (often led by Apple) change some way of doing something. The public screams bloody murder. Columnists do, too (I've been among them).

But a couple of years later we've all adopted the new technology and forgotten the old one. It's probably been years since you pined for the blistering speed of a dial-up modem and a decade since you wished you had a floppy drive.

Does that mean we're stupid and nearsighted? Not exactly. In the case of tech, there's a *cost* to each of these changes. There's a monetary cost, of course. By the time the industry abandoned the floppy-disk and CD-ROM standards, our collections of those disks were rendered worthless. And in the case of the disappearing headphone jack, there will be the cost of new wireless earbuds.

There's also a learning cost. Every time someone takes away a skill we've mastered and introduces one we haven't, that's a time-consuming challenge. There's even a convenience cost. During the transitional period to the new standard, we often have to buy and carry some bridge technology, such as external DVD drives, USB modems—or headphone-jack adapters.

Above all, though, there's a *psychological* cost to change, a helpless, primitive "Who moved my cheese?" reaction. As a species, we don't like lifestyle changes even if logic tells us that we should make them. (See also: climate change, diet, smoking.)

That's because, at its heart, change means leaping into the unknown. And the unknown—as our Neandertal ancestors approaching a dark cave could have told you—is frightening.

The big tech companies will always want to swat their public along into the future. In the end, resistance is futile—but it's also entirely understandable. SA

SCIENTIFIC AMERICAN ONLINE
WHAT LIFE IS LIKE WITHOUT A HEADPHONE JACK:
scientificamerican.com/dec2016/pogue

Illustration by Koren Shadmi

INNOVATION

2016 WORLD CHANGING IDEAS

10 BIG ADVANCES

with the potential to solve problems and improve life for all of us

The phrase "world changing" is overused. Yet how else do you capture the full world-historical influence of an invention like the transistor, or the World Wide Web, or the cellular phone? Some ideas really do bend history. It's too early to know whether carbon-breathing batteries, ingestible robots, quantum satellites, and the seven other ideas described in these pages will have a similar effect. Most plans fail, and the biggest ideas tend to carry the greatest risk. But it doesn't take long for an idea to go from laughable to inevitable. And a few of those, of course, go on to become transformative. —*The Editors*

Illustrations by Daniel Stolle

1.

CARBON-BREATHING BATTERIES

Electrochemical cells could suck carbon out of the atmosphere and turn it into electricity

Cutting greenhouse gas emissions is not enough to stop global warming. At this point, we will have to remove some of the carbon dioxide already in the atmosphere. The good news is that there are plenty of ways to do this. The bad news: those methods generally require huge amounts of energy.

The ideal carbon-sequestering technology would generate electricity rather than burn it. In a study published in July in *Science Advances,* Wajdi Al Sadat and Lynden Archer, both researchers at Cornell University, described a design for an electrochemical cell that captures carbon dioxide.

The battery's anode is made of metallic aluminum, which is cheap, abundant, and easy to work with. The cathode consists of porous carbon, which the researchers inject with a mixture of gaseous oxygen and carbon dioxide. Aluminum, oxygen and carbon dioxide react inside the battery to yield electricity and aluminum oxalate. Sadat and Archer say that over the life span of the 1.4-volt battery, their cell sequesters a kilogram of carbon dioxide for every kilogram of aluminum used.

It also turns out that the chemical by-product where the carbon ends up—aluminum oxalate—is valuable. Global demand for oxalates, which are used as cleaning and bleaching agents, is around 230,000 metric tons a year, and every ton that comes from battery by-products is a ton that a carbon-belching factory does not have to produce. With all the carbon savings figured in, the batteries capture 3.52 kilograms of CO_2 for every kilogram of aluminum used to make them. "If you factor in the major sources of CO_2, these batteries come out ahead," Archer explains.

The ideal carbon-sequestering technology would generate electricity rather than consuming it.

Archer says that they are still far from turning their design into a usable technology. First, they need to demonstrate that the technology is cost-effective and scalable. If they can achieve that, Archer envisions the batteries someday outfitting a power plant or automotive tail pipes. "This way you're not just throwing away the CO_2," he says. "You're using it."

—Annie Sneed

2.

NEW ANTIBIOTICS FROM SCRATCH

A method for designing novel compounds could help defeat drug-resistant bacteria

It's hard to imagine a world without antibiotics, but because of widespread overuse of the drugs, that's where we're headed. The Centers for Disease Control and Prevention says that in the U.S. alone, more than 23,000 people now die every year from infections that antibiotics can no longer cure. A study commissioned by the U.K. government estimated that by 2050, antibiotic resistance will cause 10 million deaths worldwide annually. Scientists have struggled to develop new drugs that can kill these superbugs. Consider the major class of antibiotics called macrolides, which treat common bacterial infections, including pneumonia, strep throat, ear and skin infections, and sexually transmitted diseases.

Researchers have tried to revamp the chemistry of these antibiotics to make them more effective against resistant strains, but they have had little success so far. The chemical structure of macrolides is difficult to manipulate, and the raw materials that go into making them are produced in large vats of industrial bacteria—not an easy process to tweak with any precision. "Chemists have been hamstrung for decades," says Andrew Myers, a professor of chemistry and chemical biology at Harvard University.

Recently, though, Myers and his team figured out a practical method for creating macrolides from the ground up. To do this, they break down the structure of macrolides into eight simple building blocks and then reconstruct them in different forms, tinkering with the chemistry as they go. In a research paper published this past May in *Nature,* Myers's group reported synthesizing more than 300 novel compounds. Tested against 14 pathogenic bacteria, the majority kept microbes at bay, and some could conquer drug-resistant strains.

Since then, the researchers have made another 500-plus new compounds, and Myers has started a company, Macrolide Pharmaceuticals, to commercialize drugs produced by the process. The group has begun work on two additional classes of antibiotics, lincosamides and aminoglycosides. Only a handful of the compounds they create will become practical antibiotics, and even those have a long way to go before they reach pharmacies. But Myers is hopeful that research such as his own will help defeat superbugs. "I have every optimism that as we continue to explore," he says, "this is only going to get better." —*A.S.*

3.

QUANTUM SATELLITES

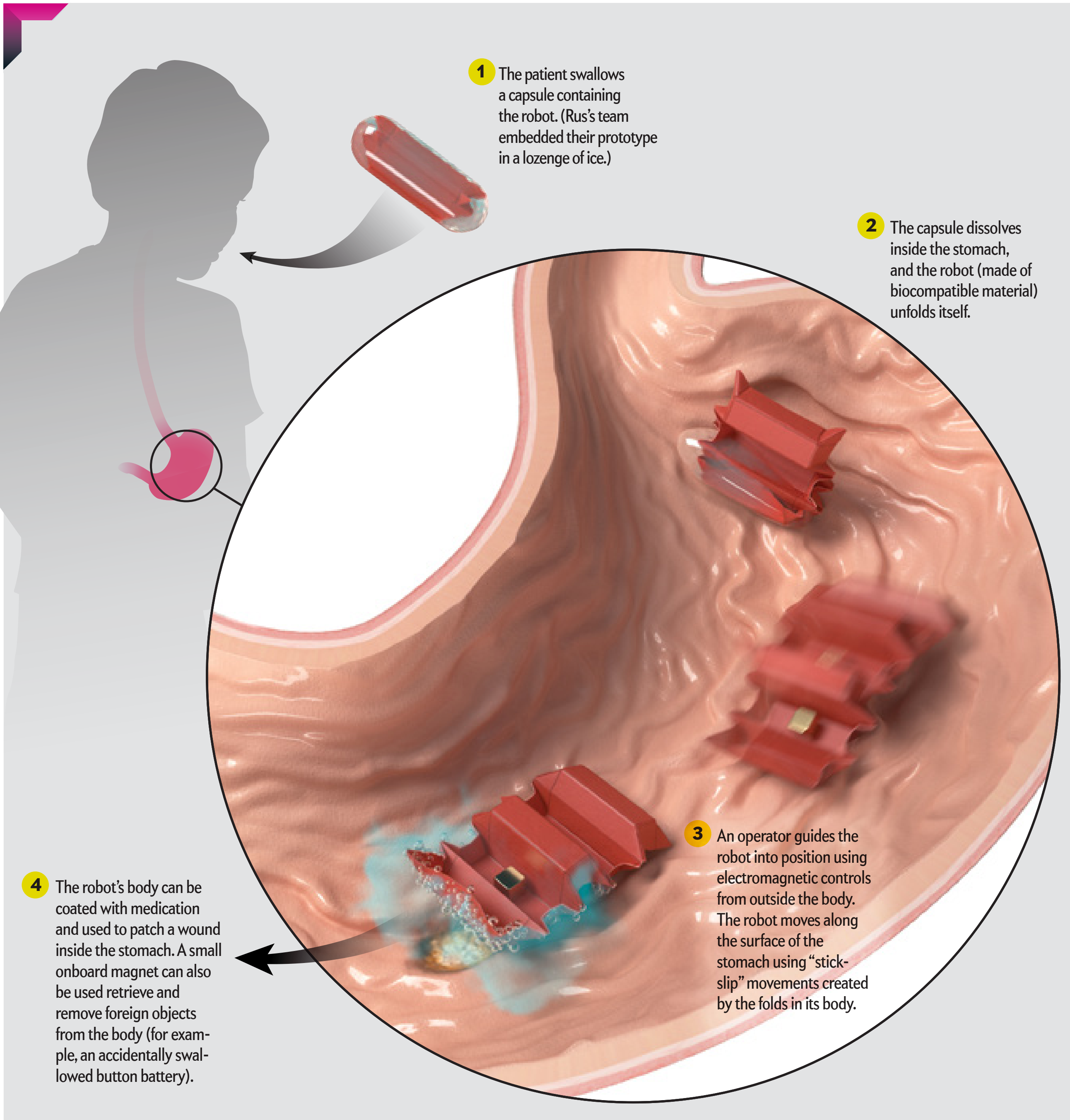
Space-based transmission of quantum cryptographic keys could make the "unhackable" Internet a reality

Perfectly secure cryptography requires no technology more exotic than pencil and paper: Choose a random string of letters and numbers to serve as the key for an enciphered message. Write the key down on a piece of paper, use it once and then burn the paper. The trick is to make sure no one intercepts or tampers with the key—and on the Internet, keys are stolen or tampered with all the time.

Quantum-key distribution (QKD) solves this problem by creating a single-use key out of entangled photons—particles of light whose quantum states are linked. Any disturbance of one particle instantaneously mirrors itself in the other one, no matter how far away. The problem with QKD is that no one has figured out how to transmit entangled photons over large distances. This past August, however, the Chinese Academy of Sciences took a big step toward solving that problem when it put the world's first quantum satellite into orbit.

The program, called Quantum Experiments at Space Scale (QUESS), is a collaboration with the Austrian Academy of Sciences. The idea is to use the satellite to transmit quantum keys to two observatories on opposite sides of China, about 1,200 kilometers apart—more than eight times farther than the current distance record. According to *Scientific American* editorial board adviser and physicist Anton Zeilinger, whose team set that record in 2012 (and who is currently collaborating with his former student Jian-Wei Pan, now QUESS's chief scientist), a space-based platform was the only option. "Tell me any location on Earth where you can look 1,000 kilometers," he says.

If the Chinese researchers set a new distance record, future satellites could provide an orbiting platform for an unhackable "quantum Internet," in which packets of encrypted data have their security vouchsafed by the laws of physics. "We hope to establish intercontinental quantum communication," Zeilinger explains. "It's not just a science-fiction idea—it's how computers in the future will talk to each other." —*John Pavlus*



SOURCE: "INGESTIBLE, CONTROLLABLE, AND DEGRADABLE ORIGAMI ROBOT FOR PATCHING STOMACH WOUNDS," BY SHUHEI MIYASHITA ET AL. PRESENTED AT THE 2016 IEEE INTERNATIONAL CONFERENCE ON ROBOTICS AND AUTOMATION, STOCKHOLM, SWEDEN, MAY 16–21, 2016

4.

INGESTIBLE MICRO ROBOTS

Remote-controlled origami robots can perform medical procedures from the inside out

The more advanced a medical intervention is, it seems, the less invasive it is to perform. For example, bariatric surgery once entailed opening a patient's abdomen from navel to diaphram; today such operations are done laparoscopically through incisions mere centimeters in size. Now researchers at the Massachusetts Institute of Technology have built a prototype robot that can perform simple procedures inside the stomach without any incisions or external tethers at all—the patient just swallows it.

Once in the digestive tract, the micro robot, encased in a lozenge of ice, makes its way to the stomach. The ice melts, and the robot unfolds like a piece of origami. The unfurled robot, which looks like a wrinkled

Illustration by AXS Biomedical Animation Studio sheet of paper, moves by virtue of strategically placed folds, slits and patches of material that expand or shrink when exposed to heat or magnetic fields; these points of movement work like joints and muscles. Surgeons pilot the robot from the outside using electromagnetic fields to act on an onboard magnet. The robot can also crawl into position by flexing the folds of its body against the walls of the stomach in what is known as stick-slip motion.

The robot's biocompatible body—partially fabricated out of pig intestine (like that used in sausage casings)—can deliver medication to an internal wound or patch it by settling onto the

The robot can deliver medication to an internal wound or patch it by settling onto the injury like a Band-Aid.

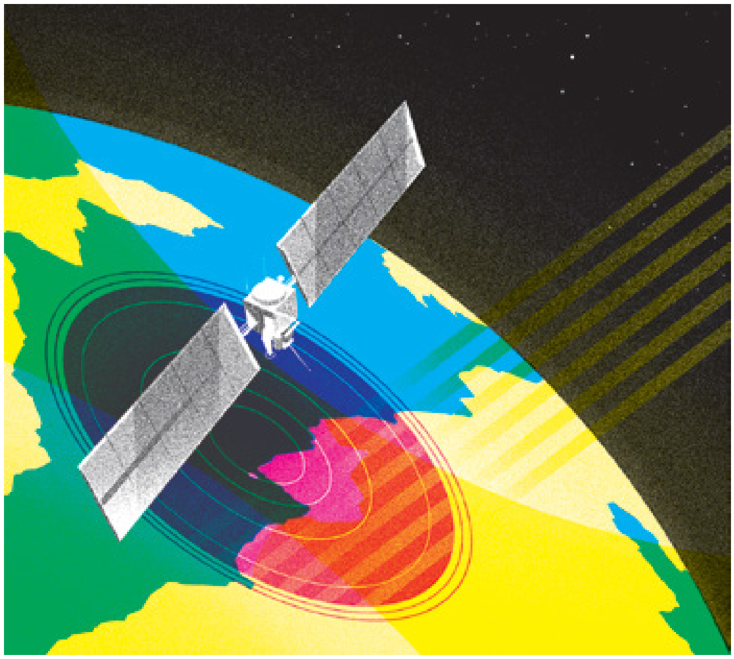
injury like a Band-Aid. The robot can also use its magnet to "pick up" and remove a foreign object, such as a swallowed button battery.

The robot has yet to be tested in humans or live animals. But M.I.T. robotics engineer Daniela Rus, whose group conducted the research, considers it a successful proof of concept for "even more capable robots" that might one day use onboard sensors to diagnose the source of internal bleeding. The ability to remove objects without traumatic surgery would be a huge leap. "My father had a kidney stone in the 1970s, and they essentially sliced half of his body open to extract this thing," Rus says. "It will take a number of years before [micro robots] become feasible, but if it does, just imagine what this method could do for these procedures." —*J.P.*

5.

POVERTY-PREDICTING SOFTWARE

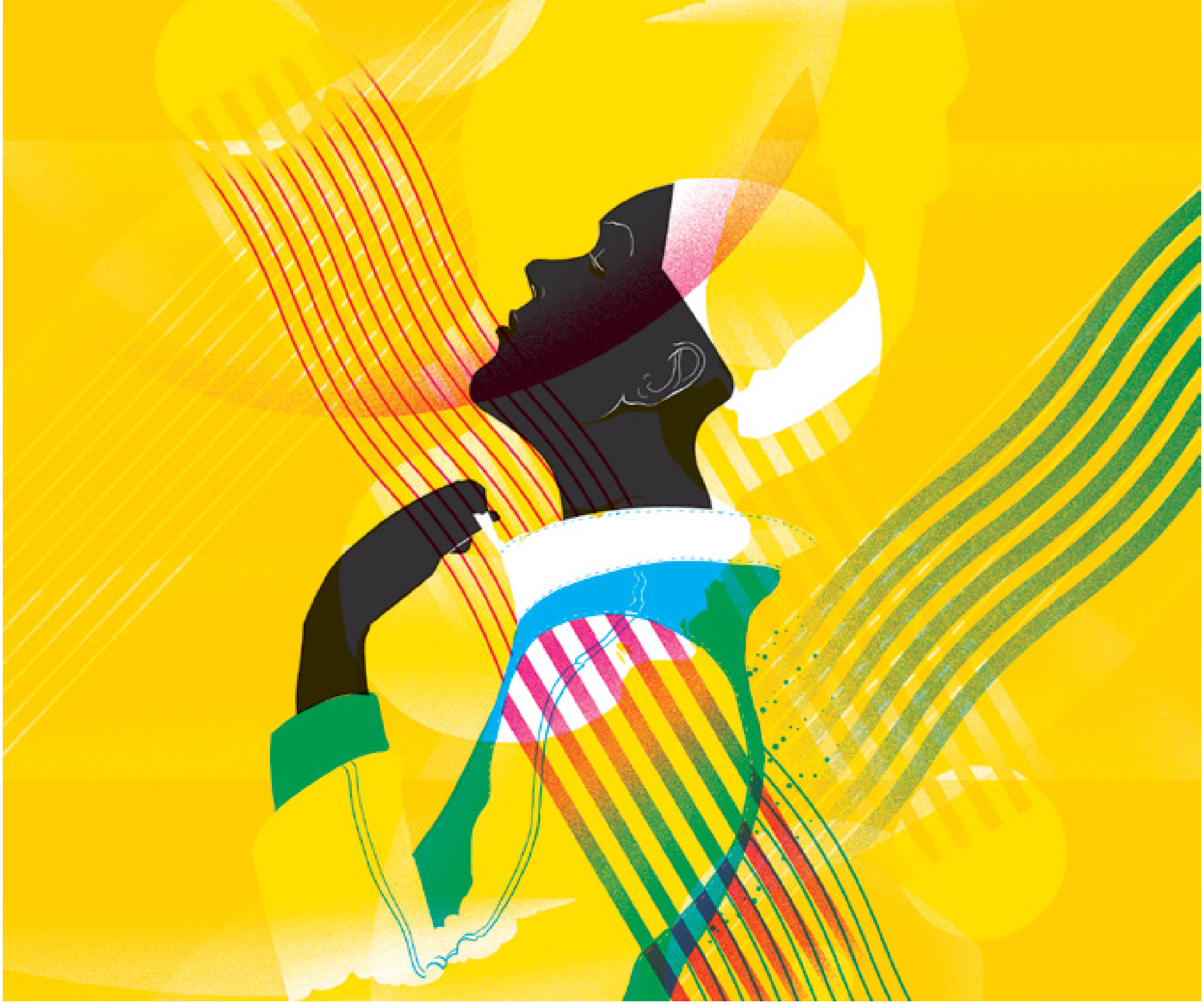
Machine-learning software analyzes satellite images to find remote areas that need help



Last year the United Nations set a goal of eliminating extreme poverty worldwide by 2030. That's an audacious target. One of the first steps—figuring out where the most impoverished people live—has proved surprisingly difficult. Conducting economic surveys in poor or conflict-prone countries can be expensive and dangerous. Researchers have tried to work around this limitation by searching nighttime satellite images for unusually dark areas. "Places lit up at night are generally better off," explains Marshall Burke, an assistant professor of earth science systems at Stanford University. But this method is imperfect, especially for differentiating between grades of poverty. From space, at night, mild and extreme poverty look the same—dark.

Burke and his team at Stanford think they have found a way to improve the study of satellite images using machine learning. The researchers trained image-analysis software on both daytime and nighttime satellite imagery for five African nations. By combining both sets of data, the computer "learned" which daytime features (roads, urban areas, agricultural lands) were correlated with different levels of night-lights brightness. "The night lights are a tool to figure out what's important in the daytime imagery," Burke says.

Once the training was complete, the software could spot impoverished areas simply by looking at daytime satellite images. When the researchers compared the results with survey data from the five African countries, they found that their method outperformed other nontraditional poverty-predicting tools, including the night-lights model. Governments and nonprofits could use the tool to determine whom to target in a cash-transfer program, for example, or to evaluate how well a certain antipoverty policy works. The researchers have plans to collaborate with the World Bank to chart out poverty in places such as Somalia. Next, Burke and his team want to use their new technique to create an Africa-wide map. —*A.S.*



6.

COOL CLOTHES

Nanoporous fabric would cool its wearers, reducing the need for air-conditioning

The hotter the world gets, the more people will turn up the air-conditioning. But cooling air requires energy, which generates greenhouse gas emissions. In the U.S., air conditioners contribute more than 100 million metric tons of carbon dioxide to the atmosphere every year.

Yi Cui, a professor of materials science and engineering at Stanford University, wants to cool people with clothing instead. Even lightweight clothes made of cotton fabric absorb infrared radiation emitted by our bodies, trapping heat. Cui and his team found that a material called nanoporous polyethylene, or nanoPE, which is used in lithium-ion batteries, lets that radiation escape. And unlike high-tech exercise clothes, which depend on perspiration to keep their wearers cool, nanoPE works with no sweat required.

NanoPE, which is roughly the same price as cotton fabric, comes in thin sheets perforated with interconnected pores ranging from 50 to 1,000 nanometers wide. Pores this size let infrared radiation escape while scattering visible light, making the material opaque. (Regular polyethylene is transparent, which is an obvious drawback for a clothing material.) A sheet of nanoPE looks like a flimsy piece of plastic—not a natural clothing material. Cui's team turned it into a passable textile by coating it with a chemical that wicks away water, sandwiching a layer of cotton mesh between two sheets of nanoPE and poking tiny holes in the fabric with a microneedle so that air could flow through it more easily. After these adjustments, Cui found that nanoPE cooled simulated human skin by two degrees Celsius more than cotton. The group reported its findings this past September in *Science.*

"If you wear nanoPE, as long as the external temperature is lower than your body temp, you'll feel cooler," Cui explains. On hot days you might still want to run the AC, but you will be able to turn the thermostat up—and research shows that raising thermostat set points by just a few degrees can cut energy use by almost half.

The team still needs to test the durability, comfort and cooling effect of nanoPE on real human skin, and the researchers have yet to determine how dyes will change its performance. If the material passes these tests, Cui envisions its being used in uniforms and scrubs for workers in factories and hospitals. *—A.S.*

7.

THE ULTIMATE VIRUS FIGHTER

A rare genetic mutation might inspire the first broad-spectrum antiviral

Viruses are notorious for evading man-made drugs, but they are powerless against a rare mutation in the gene *ISG15.* A person who possesses this mutation is better at fighting off most (if not all) of the viruses that plague humankind—but probably fewer than one person in 10 million has it. Dusan Bogunovic of the Icahn School of Medicine at Mount Sinai thinks it may be possible to develop a drug that mimics this mutation. If he is right, he may be on the verge of developing a pill that will temporarily bestow the ability to fight off a virus—any virus—without getting sick. The medication should also grant the person who takes it lifelong immunity to any strain encountered while on the drug (unless the virus mutates, as the flu does).

To figure out how the mutation suppresses viruses and how a drug might imitate it, Bogunovic and his team recruited six people with this defect, sequenced their DNA, and isolated blood and skin cells from several of them. The researchers then exposed skin cells from three of the people to multiple viruses, including influenza and herpes. After 24 hours, their cells contained orders of magnitude fewer copies of viral particles than normal cells. The reason, the team explained this past May in *Nature Communications,* is that the *ISG15* mutation knocks out a function that helps to dampen inflammation. Inflammation helps the body fight viruses, so these people "are just a little more ready than you or I for the virus that infects them," Bogunovic says. As a result, their body fights invading viruses and develops immunity before the virus can replicate enough to make them sick.

Bogunovic wants to find a drug that can mimic the effects of the *ISG15* mutation. "By tuning our system ever so slightly, we could tame the first burst of infection," he explains. Bogunovic's group is now screening 16 million compounds in search of a promising antiviral drug. Once it finds candidates, it will need to fine-tune their chemistries, perform toxicology and animal tests, and, finally, run human clinical trials. Success is by no means guaranteed. Some people with the *ISG15* mutation have occasional seizures and the beginnings of lupuslike autoimmunity; any drug would need to avoid such side effects (the researchers say taking the drug short term may help with that). Bogunovic is currently in negotiations to start a biotech company based on his research. "Nothing is impossible," he says. "It's a process, but I think a very exciting one." *—A.S.*

8.

SIGHT-READING SOFTWARE

An approach to artificial intelligence that enables computers to recognize visual patterns better than humans

If someone showed you a single character from an unfamiliar alphabet and asked you to copy it onto a sheet of paper, you could probably do it. A computer, though, would be stumped—even if it were equipped with state-of-the-art deep-learning algorithms such as those that Google uses to categorize photographs. These machine-learning systems require training on enormous sets of data to make even rudimentary distinctions between images. That may be fine for machines in the post office that sort letters by zip code. But for subtler problems, such as translating between languages on the fly, an approach learned from a handful of examples would be much more efficient.

Computers are closer to making this leap because of a machine-learning framework called Bayesian program learning, or BPL. A team of researchers at New York University, M.I.T. and the University of Toronto has shown that a computer using BPL can perform better than humans at recognizing and re-creating unfamiliar handwritten character sets based on exposure to a single example. ("Bayesian" refers to a kind of probabilistic reasoning that can be used to update uncertain hypotheses based on new evidence.)

The BPL approach to machine learning is fundamentally different than deep learning, which roughly models the human brain's basic pattern-recognition capabilities. Instead BPL takes inspiration from the ability of the human brain to infer a set of actions that might produce a given pattern. For example, it would recognize that the letter A can be built out of two angled strokes connected at the top, with a short, horizontal stroke in the middle. "The computer represents the A by assembling a simple program that generates examples of that letter, with different variations every time you run the code," says Brenden Lake, a Moore-Sloan Data Science Fellow at N.Y.U. who collaborated on the research. Bayesian processes allow the software to cope with the uncertainty of re-creating unfamiliar letters out of smaller, previously known parts (for example, the horizontal stroke in an A).

This kind of machine learning is more versatile, as well as more efficient. The same processes that BPL software uses to deconstruct and then re-create an unknown letter could someday power AI applications that can infer cause-and-effect patterns in complex phenomena (such as the flow of a river) and then use them to address completely different systems. Human beings regularly employ this kind of abstract "lateral thinking"; BPL could unlock similar capabilities for computers. "We're trying to get computers to be able to learn concepts that can then be applied to many different tasks or domains," Lake says. "That's a core aspect of human intelligence." *—J.P.*

9.

PAPER DIAGNOSTICS THAT COST PENNIES

Cheap, rapid screening for diseases such as Ebola and tuberculosis could save lives in remote and impoverished places

A patient checks into a rural African clinic with a high fever. The diagnosis could be anything from mild typhoid to Ebola. Even if laboratory blood tests are available, it will take days to get results. What is a doctor to do: Prescribe antibiotics or order a quarantine?

Researchers have been working for a decade on quick, cheap paper diagnostics (think home pregnancy tests) that could save lives in such situations. The first generation of those tests is now inching toward commercialization. The nonprofit organization Diagnostics For All is awaiting regulatory approval to deploy a blood-based liver-function test in Africa. The Bill & Melinda Gates Foundation–funded Intellectual Ventures in Bellevue, Wash., is working on an ultrasensitive malaria test, as well as a urine-based tuberculosis diagnostic tool. Paul Yager, a bioengineering professor at the University of Washington, is developing a sensitive test for the Ebola virus protein in blood. None of these devices costs more than a few dollars or requires special training.

At the heart of these diagnostic tools are strips of paper that are either engraved or overlaid with patterns that split, concentrate and mix fluids. Paper naturally wicks blood, urine and other fluids, so samples flow through the devices under their own power. The patterns steer the fluid through the dilutions and reactions necessary for identifying a pathogen or disease marker. For example, Diagnostics For All's liver-function test contains a filter that screens out red blood cells, allowing plasma to flow into a bottom paper layer loaded with reagents that combine with an enzyme that indicates liver damage. A color change indicates the patient's enzyme level.

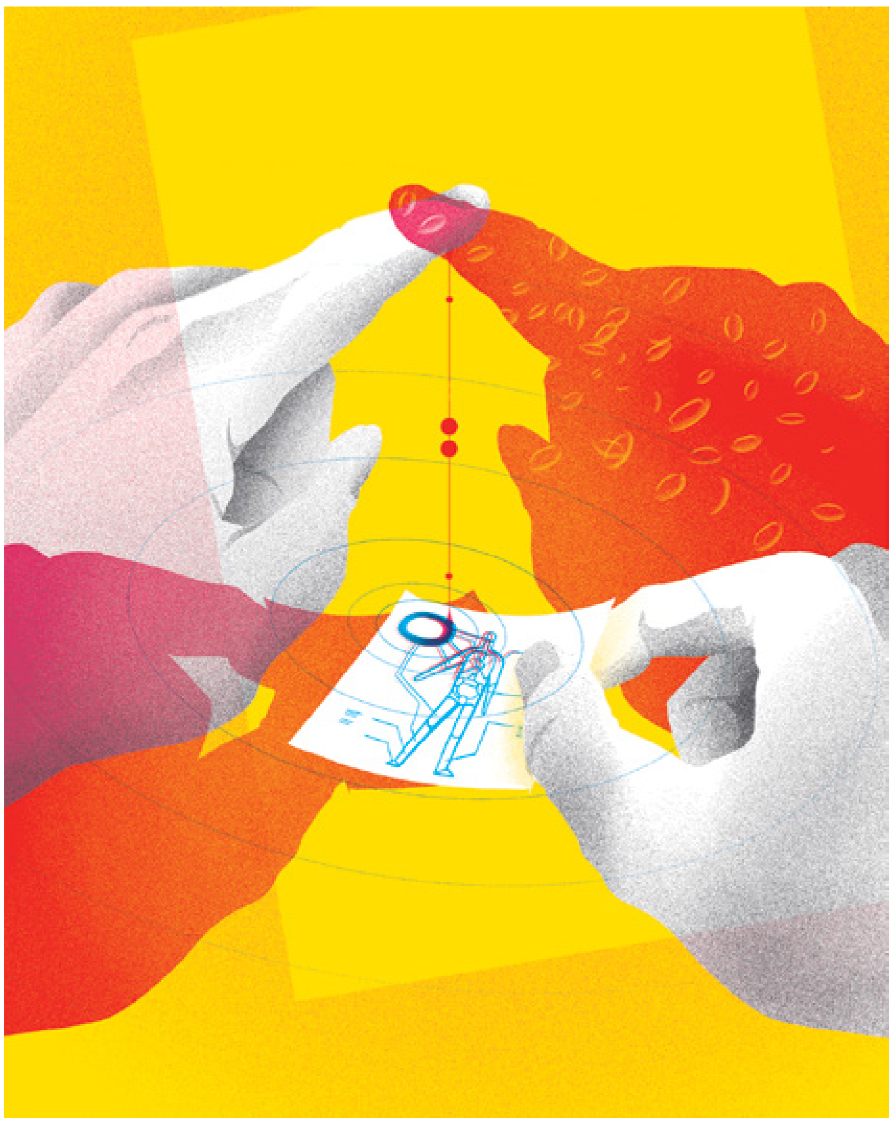
The first generation of paper diagnostics will generally detect disease by spotting molecules produced by the infected body or by the culprit microbes themselves, but tests that directly detect the DNA of pathogens could follow. These so-called nucleic acid tests would allow doctors to accurately identify diseases in their earliest stages. Yager, Harvard University chemistry professor George Whitesides and other researchers are independently pursuing paper-based nucleic acid testing. Yager is developing a nucleic acid–based home Zika virus test and is

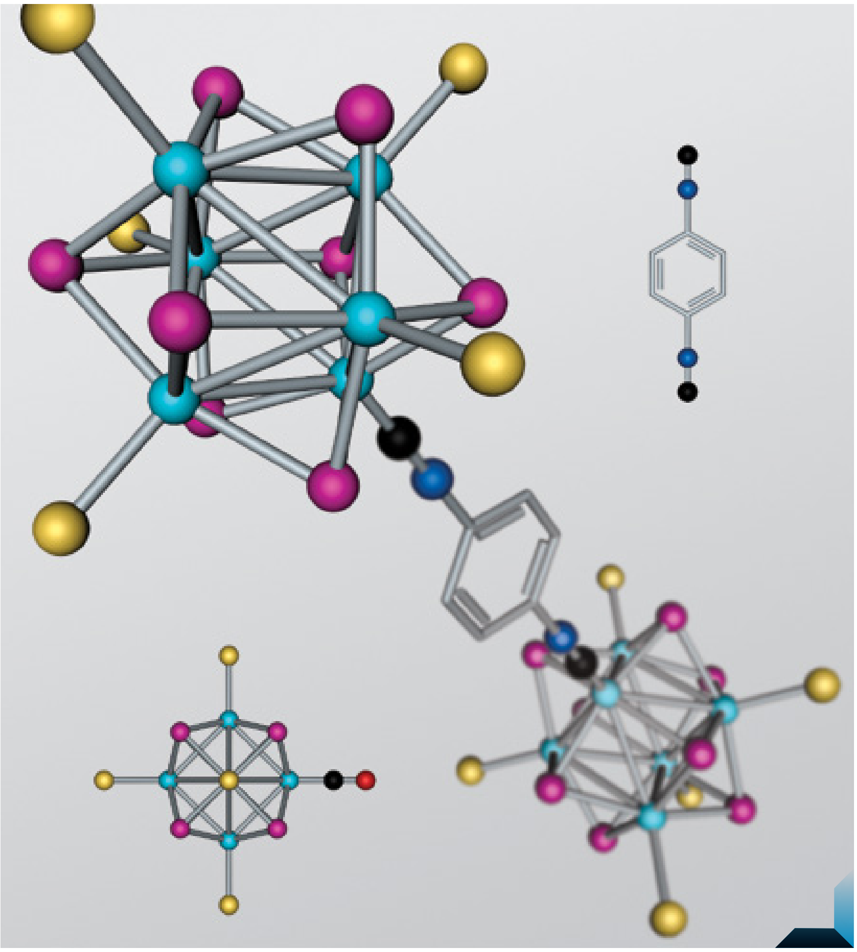
Should a doctor order antibiotics or a quarantine?

applying for funding for faster, cheaper tests for Zika, dengue and yellow fever.

Technical challenges remain, but researchers say the biggest barrier is financial. Pharmaceutical companies see little profit in devices that cost pennies, so most funding comes from governments and private foundations. "We and others have shown that the technology works," Whitesides says. "A lot depends on whether we can get over the last hump of commercialization."

—Prachi Patel





SUPERATOMS are clusters that behave like single atomic units; supermolecules, such as the cobalt-selenium complex above, combine superatoms and could yield new, useful materials.

10.

SUPER-MOLECULES FROM SUPERATOMS

A way to design new molecules and materials that the periodic table does not allow

The periodic table may look like it has plenty of elements, but chemists and materials scientists would like more, thank you. That is because in the quest to design synthetic materials with unusually useful properties—say, a siliconlike superconductor with the biodegradability of wood—nature's cookbook has its limits. "Oftentimes you'll want an atom that actually doesn't exist," says Colin Nuckolls, a professor of chemistry at Columbia University. Molecules built out of so-called superatoms—clusters of atoms that behave like single elemental units—could fill this need. Superatoms can be given electronic and magnetic properties that would be difficult or impossible to achieve using natural combinations of elements. But although chemists have known for decades how to create superatoms, a reliable way of linking them into larger structures has proved elusive.

Now Nuckolls's team has discovered a method for constructing "designer molecules" out of superatoms. These synthetic structures could mimic the properties of naturally occurring molecules while giving materials scientists the ability to "tune" their properties to match particular purposes. "You can easily vary chemical or magnetic properties of superatom molecules in ways you wouldn't be able to do with just atomic structures," Nuckolls says. "It's like adding another dimension to the periodic table."

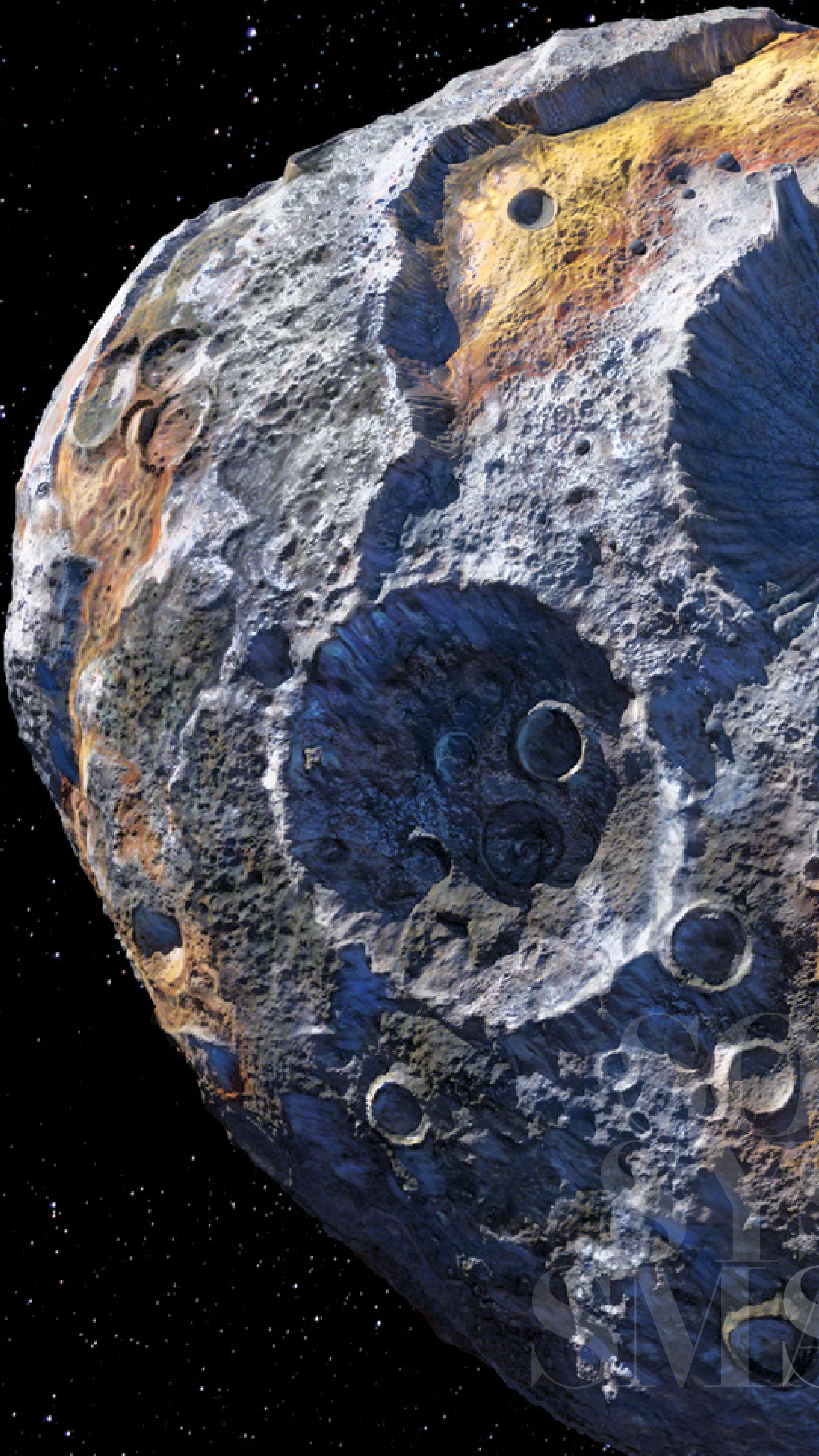
Walter Knight and his collaborators at the University of California, Berkeley, discovered superatoms in 1984 by synthesizing clusters of sodium atoms whose outer shell of electrons behaved like the shell of a single atom, enhancing magnetic and reactive properties. Since then, scientists have made superatomic clusters from aluminum, platinum, rubidium and other elements. But to combine superatoms into larger molecules, scientists needed to figure out the special chemical rules that superatoms follow, which differ from those of their cousins in the periodic table.

Electrons naturally arrange themselves around the nucleus of an atom in an orderly fashion known as *Aufbau*, occupying lower energy levels before higher ones. (*Aufbau* means "building up" in German; the principle was introduced in the early years of quantum mechanics.) Based on an initial discovery by graduate student Anouck M. Champsaur, Nuckolls's team pieced together the beginnings of an *Aufbau*-like principle for making synthetic molecules out of superatoms.

So far the team has constructed molecules from pairs and trios of cobalt-selenium superatoms. But Champsaur and Nuckolls believe that a superatom *Aufbau* will enable the synthesis of more exotic materials with potential applications in flexible sensors, smart clothing and high-efficiency batteries. Chemistry textbooks won't need to update their periodic tables, Nuckolls says: "That would be alchemy." But superatom molecules, he says, are "a way of getting more than nature gave you." —*J.P.*

SOURCE: "BUILDING DIATOMIC AND TRIATOMIC SUPERATOM MOLECULES," BY ANOUCK M. CHAMPSAUR ET AL., IN *NANO LETTERS*, VOL. 16, NO. 8; AUGUST 10, 2016

Illustration by Kenneth Eward



ASTRONOMY

Our neighborhood of planets was not created slowly, as scientists once thought, but in a speedy blur of high-energy crashes, destruction and rebuilding

By Linda T. Elkins-Tanton

METAL WORLD: Asteroid Psyche, shown in an artist's conception, may be the iron-nickel core of an early planet precursor.

SOLAR SYSTEM SMASHUP

Linda T. Elkins-Tanton, a planetary geologist specializing in the evolution of terrestrial planets, is director of the School of Earth and Space Exploration at Arizona State University.

I WAS WALKING OUT OF A CLASSROOM AT THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY, WHERE students and I had been talking about the way planets form, when I was stopped by my colleague Ben Weiss. He studies magnetism in space rocks, and he was very excited. Weiss pulled me down the hall to his office to show me new data on one of these rocks, a meteorite called Allende. It was information that could change almost everything planetary geologists thought about the solar system.

It was 2009, and that fall Weiss's research team had shown that Allende—which crashed into Earth in a huge fireball in Mexico in 1969 and contained some of the oldest known material in our system—harbored signs of an ancient magnetic field in its rock. The discovery was a surprise. This kind of field, astronomers thought, was made only by a magnetic dynamo of intensely hot, flowing liquid metal inside a planet, the way Earth's magnetic field is produced by liquid iron spinning in the planet's core. But Allende was supposed to be a fragment from a parent planetesimal—an early, nascent planet—that had been only slightly warm. Scientists presumed it had never gotten hot enough to melt the metal it contained. How, then, Weiss wondered, could this ancient piece of our solar system have become hot enough to create a magnetic dynamo?

My students had just been pelting me with questions about planetary evolution, challenging me to rethink some textbook wisdom, so I happened to have the bare bones of a new idea that might help answer Weiss's question. I walked over to his whiteboard and began sketching it out.

Planetesimals had long been known to contain short-lived, unstable aluminum atoms radiating excess nuclear energy. This radioactive isotope is called ^{26}Al, and when it decayed, that excess energy could have heated planetesimals. Conceivably, the heat from ^{26}Al in Allende's parent body could have climbed so high that the object actually melted from the inside out. Metal within the body would have separated from silicate minerals in the rest of the rock and formed a liquid core that started to spin as the space rock rotated, creating a magnetic dynamo. Meanwhile the outside of the planetesimal would have been chilled by the cold of space, and cold rock and dust from our solar system's primitive disk would have kept adding to this unmelted rind.

This idea that early building blocks of the solar system contained so much energy was not the story I had learned in high school. Textbooks often still say that the solar system formed in a quiet, stately manner. That creation, 4.567 billion years ago, was thought to be an orderly, civilized process, like a minuet: the gas and dust of a molecular cloud spun down into a disk around a growing young star, and the gas and dust coalesced into many little boulders, each one of which gradually grew to tens to hundreds of kilometers in diameter. These planetesimals themselves then rammed together to form larger bodies, each perhaps the size of Mars, called planetary embryos. Only after that did the temperature in this space nursery pick up. These embryos, which in growing had gained gravity strong enough to begin clearing their orbits of surrounding debris,

IN BRIEF

Slow and steady growth, from small particles to large planets, was the way scientists envisioned the evolution of the solar system as recently as five years ago.

Recent analyses of meteorites, remnants of the system's birth, imply instead that the system came from chaotic collisions, melting and reconstruction.

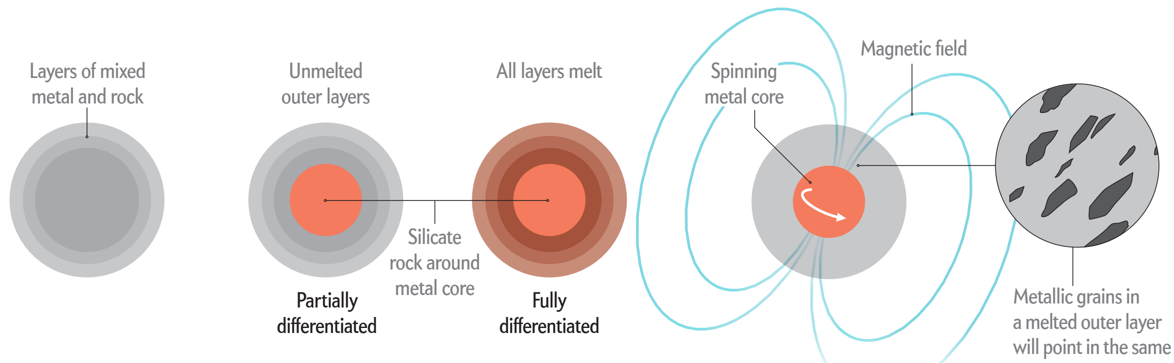
Scientists plan to send a spacecraft to Psyche, a strange all-metal asteroid that may be a naked chunk of an early planet core, to verify this idea.

PRECEDING PAGES: COURTESY OF ASU AND PETER RUBIN *Iron Rooster Studios*

Solar System Building Blocks

Planets like Earth and its neighbors got started when the cloud of gas and dust around our sun generated lumps known as planetesimals (*top*). These bodies were once thought to be quiet planetary seeds. But researchers now believe they crashed around and jump-started high-energy processes that gave rise to true planets (*bottom*).

Inside a Planetesimal

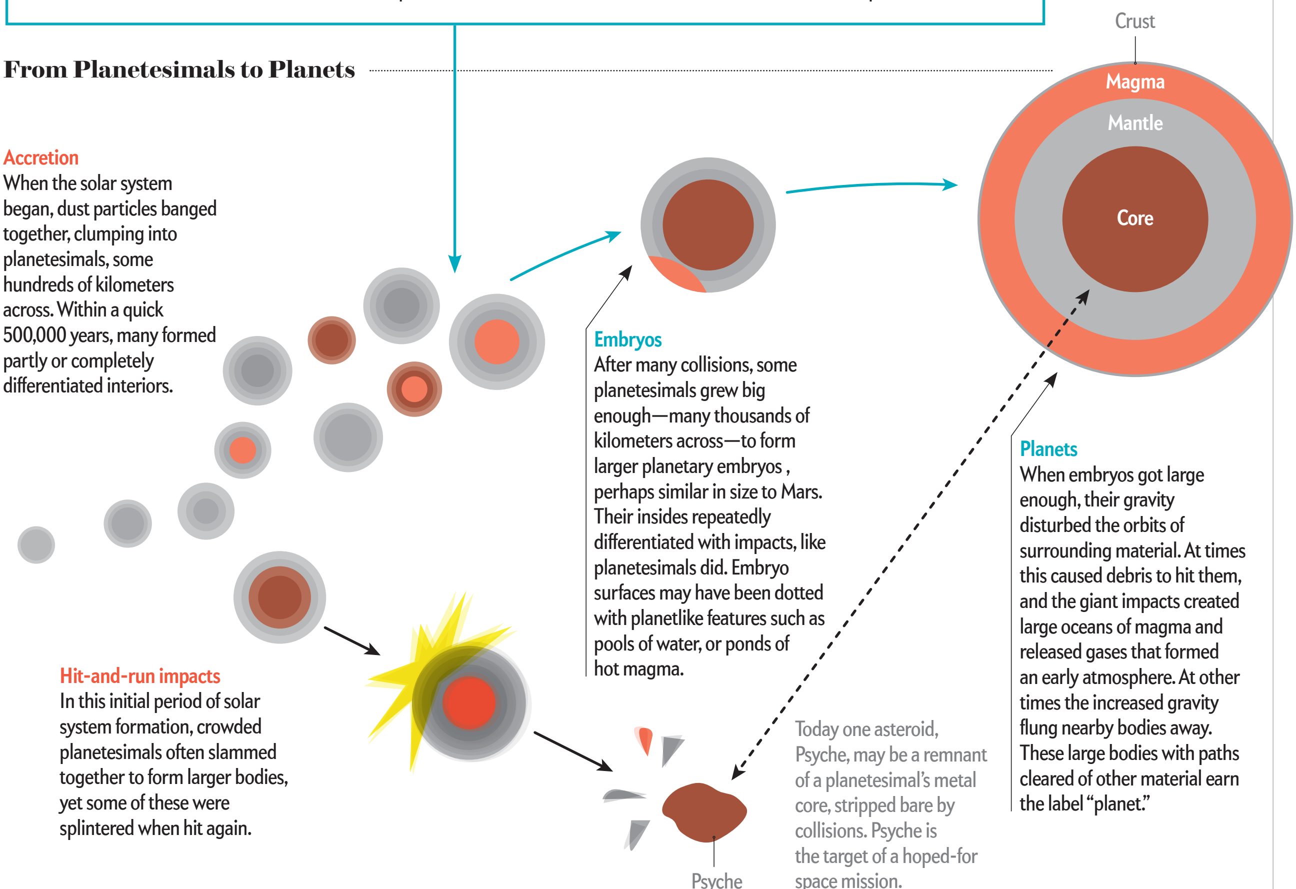


Undifferentiated planetesimal
These rocks were 10 to a few hundred kilometers in diameter and contained radioactive elements that heated their innards. They had an onionlike structure.

Differentiated planetesimals
Radioactive elements created more heat, and the body melted from the inside out. Denser iron-nickel metal sunk inward. Sometimes an outer rind was unaltered. All differentiated planetesimals had a liquid-metal core.

Magnetic field formation
Metal in motion can become a magnetic dynamo, which happened when planetesimals and their liquid metal cores started to spin. These cores generated magnetic fields pointing in particular directions, like Earth's field points north.

From Planetesimals to Planets



Accretion
When the solar system began, dust particles banged together, clumping into planetesimals, some hundreds of kilometers across. Within a quick 500,000 years, many formed partly or completely differentiated interiors.

Hit-and-run impacts
In this initial period of solar system formation, crowded planetesimals often slammed together to form larger bodies, yet some of these were splintered when hit again.

Embryos
After many collisions, some planetesimals grew big enough—many thousands of kilometers across—to form larger planetary embryos, perhaps similar in size to Mars. Their insides repeatedly differentiated with impacts, like planetesimals did. Embryo surfaces may have been dotted with planetlike features such as pools of water, or ponds of hot magma.

Today one asteroid, Psyche, may be a remnant of a planetesimal's metal core, stripped bare by collisions. Psyche is the target of a hoped-for space mission.

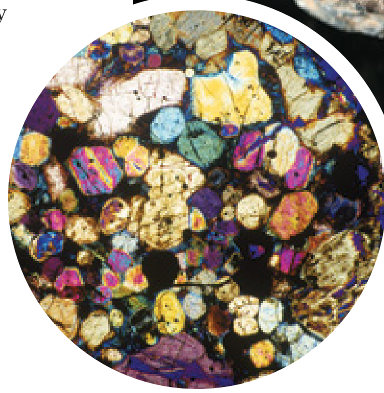
Planets
When embryos got large enough, their gravity disturbed the orbits of surrounding material. At times this caused debris to hit them, and the giant impacts created large oceans of magma and released gases that formed an early atmosphere. At other times the increased gravity flung nearby bodies away. These large bodies with paths cleared of other material earn the label "planet."

Illustration by Jen Christiansen

then collided together and grew into planets. Eventually components in these planets separated into the familiar churning metal core and a silicate mantle—hot, wildly volcanic places, antithetical to life.

That's the old view. By the time Weiss and I began pondering Allende, some other data, too, indicated that the earliest solar system was really a place of rapid and violent change. Now that tame sequence of dust to boulders to planetesimals to embryos to planets is being replaced. Actual planetesimal formation, once surmised to take place over hundreds of millions of years, happened in just about three million years. If the age of our solar system, in human time, is now a day, this growing up happened during the very first minute. More energy in the early small components—energy like that provided by the aluminum heating and early collisions—means they did not have to wait and grow before developing different layers. Relatively minute planetesimals could host processes previously believed to be confined to planets, from melting and degassing to the creation of magnetic dynamos and volcanism.

And things in this system did not simply grow from small to large. Often large things blew apart into small again. If planet-size spheres formed in those early years, through collisions of these smaller high-energy bodies, then glancing, hit-and-run blows among planetesimals sometimes stripped or destroyed them instead. Their debris could hit other spheres, enlarging them to planet size. Planets could be built, torn asunder and rebuilt in just 10 million years or less.



ANCIENT MAGNET: A fragment of a meteorite called Allende (*shown in photograph* and *micrograph cross section*) holds signs of magnetism created by planet precursors.

THE DISAPPEARING DISK

PLANETARY SCIENTISTS such as me have pieced together this new, three-ring circus vision of the active young solar system with great help from new tools for calculating the ages of meteorites, as well as the ages of planetary dust clouds—similar to our primordial solar system—elsewhere in the cosmos.

Over the past 10 to 15 years, scientists have developed instruments capable of measuring the elements that make up space rocks to parts per million or even less. Because we have a good idea of how long it takes radioactive elements to decay into their daughter elements, such measurements allow us to date when the planets and planetesimals that shed these fragments formed and changed. Teams all over the world—notably Alex Halliday, formerly at the Swiss Federal Institute of Technology Zurich and now at the University of Oxford; Thorsten Kleine of the University of Münster in Germany; Stein Jacobsen of Harvard University; Mary Horan and Rick Carlson, both at the Carnegie Institution for Science; and Richard Walker of the University of Maryland—began measuring collections of meteorites. The work made clear that planetesimals formed within the first few million years after the dusty disk began to cool, that many of our terrestrial planets could have formed within the first 10 million years, and that even most of Earth probably formed and differentiated into a core and mantle by a few tens of millions of years.

Other avenues of research yielded similar results. With ever improving telescopes, we can see young stars growing in other parts of our Milky Way galaxy, and in some cases, we can see the dust and gas disk from which a star and its planets grow. By estimating the ages of stars orbited by planets and comparing those measures with estimates for stars surrounded only by disks of dust and gas, researchers determined about 10 years ago that these disks last, on average, only three million years.

Planetesimals, therefore, have just three million years to grow on average. Any dust and gas not accreted onto rocks by then is lost into the star or out into space, and no more material for planet building is available. Considering that theorists used to think accretion took hundreds of millions of years, this is quite an acceleration!

More evidence for this timing comes from using the decay of radioactive elements like a clock, which ticks away at a steady rate as one element turns into another. The new instruments gave teams throughout Europe and the U.S. enough precision to measure these elements and thereby learn how long that clock had been ticking. Meteorites that have fallen to Earth contain those elements. Most are pieces of asteroids, which themselves are primitive remnants of planetesimals. (Some other meteorites are from the moon, some are from Mars and others are from bodies not yet identified.)

One radioactive isotope of the element hafnium prefers to stay in silicate minerals, such as those in Earth's mantle. But it decays to an isotope of tungsten, which combines readily with metals that make up planet cores. This decay happens on a regular schedule: half the hafnium turns into tungsten in nine mil-

DETLEV VAN RAVENSWAAY *Science Source (top)*; MICHAEL ABBEY *Science Source (bottom)* lion years. This system gives us the timescale of metal-silicate (core-mantle) differentiation of planets and planetesimals: metal core formation scavenges tungsten from the silicate mantle and carries it into the growing core. Any hafnium stays happily in the mantle and keeps on decaying into tungsten, which then remains in the silicate mantle if no further core formation occurs. When scientists measure the ratios of hafnium to tungsten in meteorites, the amount of that tungsten isotope in them gives the time since core formation.

Such isotopic measurements of iron meteorites—many of which presumably hail from the metallic cores of planetesimals—show that their parent bodies formed within just 500,000 years of the first solids condensing from our protoplanetary disk of dust and gas. That time is less than 10 seconds into our putative 24-hour solar system. If iron meteorites are core fragments of planetesimals smashed apart by impacts, then planetesimals must have actually formed, melted and created iron cores within that tiny period.

GROWTH SPURT

WITH EXPERIMENTAL DATA firmly showing that the solar system formed much more quickly than textbook scenarios indicated, scientists who study it now had to explain how planets came into being so quickly. That put the ball in the theorists' court. How can dust and pebbles just microns to centimeters in diameter, all orbiting around our young sun, clump together to form bodies up to 10 million times larger (100-kilometer planetesimals) in just 500,000 years?

The answer is not obvious. Standard physics says that small clumps of dust that collide can readily stick together through electromagnetic forces, much as static electricity creates clumps of household dust. The energy absorbed as a result of compression and loss of porosity during collisions also helps clumps stick together rather than bouncing off or breaking apart. As the clumps grow, though, they reach what is called the meter barrier. Before they reach a meter in diameter, these growing boulders become too large to stick by electromagnetic forces and too small still to stick through gravitational attraction. Impacts even at very low speeds cause these conglomerates to destruct rather than accrete. Yet we know that such materials must be able to grow from meter size to planetesimal size—the planet we stand on today is a testament to that. So some other processes must have been at work.

Several ideas for how growth beyond the meter barrier occurs have been proposed. Most hypotheses involve concentrating material in the protoplanetary disk through various types of turbulence that slam particles together. Such whirlpool-like forces might include phenomena called Kelvin-Helmholtz eddies, which develop between the gas and dust layer of the disk and could effectively crush regions of material together into larger bodies. Much of that work has been pioneered by Anders Johansen, now at Lund University in Sweden. Hal Levison of the Southwest Research Institute and Johansen have separately worked on a newer model, called pebble accretion. His calculations indicate that even the smallest pieces of dust and clumps can be gravitationally diverted over several orbits to add to a growing planetesimal and can do so fast enough to build planetesimals early in the life of the solar system.

MELTING IN A FREEZER

NO KIND OF CRUSHING, however, could have caused the planetesimals to differentiate into mantles and cores. If planetesimals were first formed of primordial disk material in which metals and silicates were intimately mixed, then only high temperatures and at least partial internal melting would allow the metal to sink to the interior and form a core. Calculations show that slamming these relatively small bodies together would not provide enough energy to melt them. Consequently, researchers were left wondering where that melting energy—within the vast freezer of chilly space—came from.

This is where ideas about the radioactive aluminum come in. Each time one of these atoms decays, it gives off a little burst of heat. These tiny quanta of heat could have added up to a powerful energy source in the early solar system. Because aluminum is one of the six most common elements in stony material (the others are silicon, magnesium, iron, oxygen and calcium), ^{26}Al, which has a half-life of approximately 700,000 years, could easily have heated at least some planetesimals to a melting temperature.

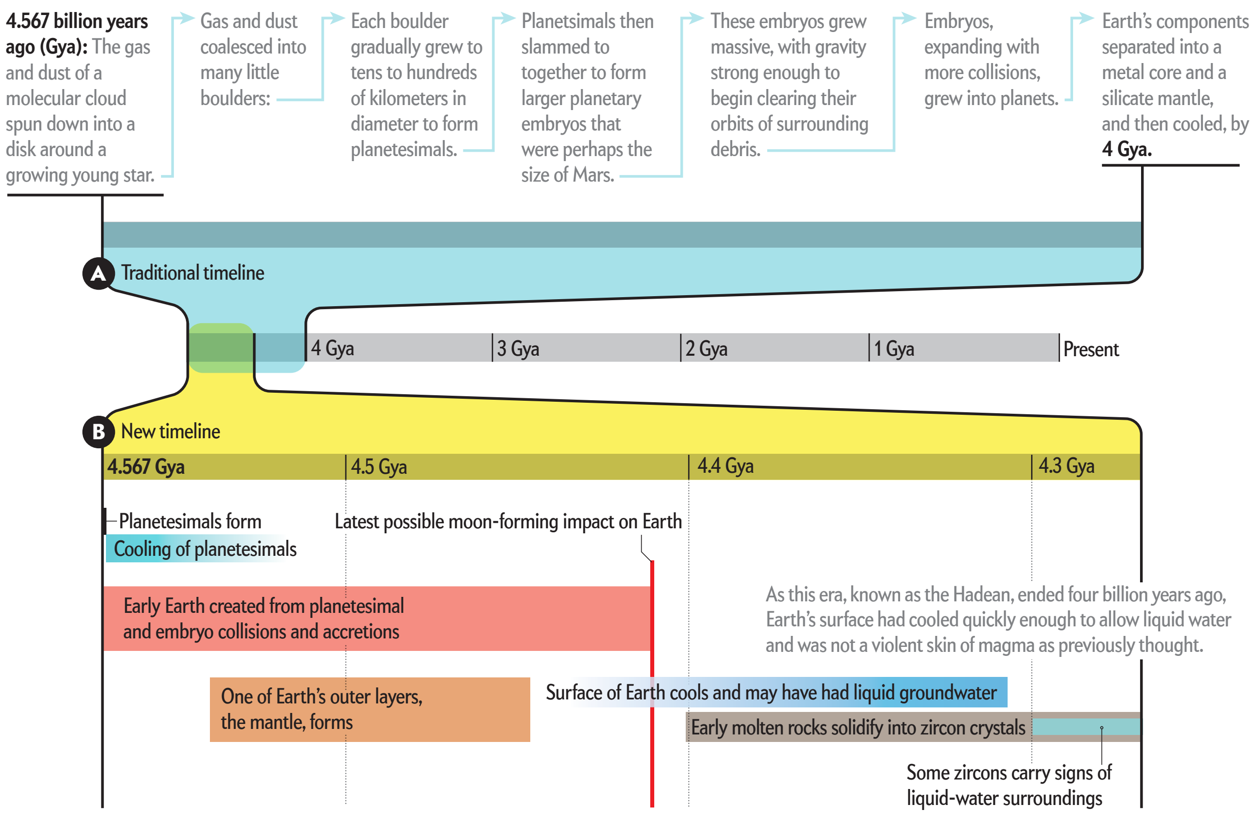
With experimental data firmly showing that the solar system formed much more quickly than textbook scenarios indicated, scientists had to explain how planets came into being so quickly. That put the ball in the theorists' court.

But what would have kept them from melting completely, considering that the new observations strongly indicate that some of these planetary seeds had unmelted rinds on the outside? Size is part of the answer. In the case of Allende's parent planetesimal, to reach melting, the rocky body would have needed to be massive enough so that its interior produced heat faster than its exterior radiated it away. A larger body can get hotter inside than a smaller body can because it has a greater heat-producing volume compared with its heat-releasing surface. But the short half-life of ^{26}Al means this growth had to be quick. To retain enough heat for the melting pattern we envisioned, Allende's parent planetesimal would have grown to 10 kilometers or more in radius within about two million years of the first solids in the solar system (the equivalent of the first 37 seconds of our 24-hour solar system)—and we think it may have grown to as much as 200 kilometers in radius.

It had been thought that planetesimals either melted entirely or remained primitive. But Weiss and I were suggesting a hybrid, where the most primitive material in the solar system encased a

Speeding Up Construction

Scientists used to think the formation of planets in our solar system was a slow, steady process that stretched over 500 million years, beginning at about 4.5 billion years ago **A**. New evidence from meteorites that fell to Earth, decay rates of radioactive elements and observations of dust around stars indicate our system—including a nascent Earth—got started much more quickly **B**, within three million years, in a high-energy blur of protoplanetary crashes and rebuilding.



planetesimal that had melted inside—an outer rind as well as a melted core. This made sense because the Allende meteorite—with its record of a magnetic field caused by a heated interior—consists of unheated, primitive material alone. The only place it could come from would be a cool outer rind. Allende's parent planetesimal retained this primitive unmelted surface rind because it was chilled by the coldness of space and because dust in the cool protoplanetary disk continued to attach to it over time. Unchanged by heating, the rind was able to maintain a record of the magnetic field produced by the inner part of the planetesimal's structure, the melted core and its magnetic dynamo.

We were not the first to have thought of partial differentiation. Geologist John Wood drew a similar structure by hand in his Ph.D. thesis at M.I.T. in 1958—but no one had ever been heretical enough to say that the poster child for primitive unmelted meteorites, Allende, could have come into existence in this way or that the process was common, indeed formative, at the beginning of our solar system.

Now it does appear common. Researchers have found that at least four other meteorite parent bodies hosted magnetic core dynamos. At the same time, other possible sources of the magnetization have been ruled out: Allende and its fellows were not magnetized by a field produced in the sun, nor by the dusty disk itself, nor by transient plumes around impacts. If the earliest solar system was truly populated by hundreds or even thousands of differentiated planetesimals, zipping around and generating intense heat and magnetic dynamos like tiny Earths, it implied the entire infant system contained a great deal more heat than geologists had ever thought.

A CROWDED FIELD

OTHER IDEAS have also weakened the traditional notion of linear planet growth from small to large. For years, for the sake of simplicity and numerical tractability, all simulations of planet formation assumed that in every collision of planetesimals, all the material from both colliders combined to form a new, bigger body. This merging occurred even as planetesimals were forming from dust. But recently new understanding and new approaches to model-

Graphic by Jen Christiansen

ing the collision process have been pioneered by Erik Asphaug of Arizona State University. Some collisions are constructive, Asphaug found, and produce larger bodies. But other crashes can be destructive, with the collider stripping material from the target body and continuing on its way to do more damage elsewhere.

Only at about 10 million years of age did bodies really get bigger and stay big. What gave them enough stability to survive? Again, the answer seems to be size. As planetesimals collided and formed larger planetary embryos, their mass and therefore gravity became larger. The gravity was great enough that whenever their orbits brought them near another object, that object was either drawn in and accreted through the pull of gravity or was flung away as its orbit was changed. Thus, these growing planets began to clear out their orbits, which is one of the criteria for being properly called a planet. Smaller bodies had fewer and fewer refuges where their orbits could remain stable and unperturbed by growing planets; the asteroid belt became one of the safe havens left to them.

We wanted to explore a place that could prove or overturn hypotheses. The best destination, we had decided, was a world made out of metal: the metal asteroid Psyche. There is nothing quite like this place, at least nothing close enough to reach in a reasonable amount of time.

MISSION TO A METAL WORLD

WEISS, ASPHAUG AND I and others would like to learn how our own planet's structure and composition came into being out of this energetic, often chaotic environment. But we cannot, despite the science fiction of popular movies or Jules Verne novels, get a good look at Earth's core. It is too deep and has pressures too high to sample directly.

But perhaps one particular asteroid, a remnant of an ancient planetesimal, might be a decent stand-in. About four years ago several of my colleagues and I began to design a space mission to explore this possibility. We gathered in the Left Field mission-formulation room at the NASA Jet Propulsion Laboratory. This room is designed for creativity. It has shelves full of drawing and building materials such as cardboard, wheels, wire, Legos, paper, markers and foam. It is a good room to think about something completely new, and that is what we were trying to do. We wanted to explore a place that could prove or overturn hypotheses. The best destination, we had decided, was a world made out of metal: the metal asteroid Psyche.

There is nothing quite like this place, at least nothing close enough to reach in a reasonable amount of time. Psyche is one of the largest asteroids, about 200 kilometers in diameter, and is located between Mars and Jupiter. All the physical measurements we have—from radio telescopes bouncing waves off the body—indicate that it consists almost solely of iron and nickel. Psyche looks like it is a stripped-naked planetesimal core, a last remnant of the hit-and-run collisions that disrupted bodies in the early solar system. The orientation of particles in Psyche, like tiny magnetic compass needles, might tell us whether it had a magnetic dynamo. There might also be some remnants of its rocky exterior that tell us what the deep mantle of planetesimals looked like. If there were surface impacts on the naked metal, the splashes might have produced sharp metal cliffs that froze before they could fall back to the surface.

Each of us in the mission room brought a particular set of skills to the table: Weiss, his specialty of measuring magnetic fields in meteorites; William F. Bottke, the dynamics of orbiting bodies; Asphaug, the effects of collisions; Bruce Bills, calculating the gravity field of a body; Daniel Wenkert, managing data and operations. Damon Landau calculated trajectories; he is an interplanetary travel agent. John Brophy organized our deliberations, and I brought my knowledge of compositions, melting, solidification and differentiation processes.

The energy in the room rose to a heady peak. There was no e-mail checking, and there were no conversational pauses. We were united in our excitement over true exploration: humankind has never visited a metal body, and we do not even know what it will look like.

Now, years later, those days of playing with foam and Legos have given way to an organized push by a team of about 75 people. We proposed a small spacecraft, powered by a combination of solar cells and an ion drive and carrying a magnetometer to detect magnetic fields, a gamma ray spectrometer to identify elements and two cameras. Our proposal made it through NASA's initial selection round in 2015. The agency intends to announce its selections this month. If we do not make the final cut this year, we will continue developing our plans for the next group of NASA missions. And if all goes well, we will visit this strange remnant of planet building in 2021. ■

MORE TO EXPLORE

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scientificamerican.com/magazine/sa

VACCINES

HIV'S ACHILLES' HEEL

Investigators hope that a three-part protein that mimics a key part of HIV particularly well could lead to a long-awaited vaccine

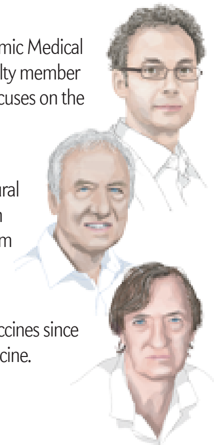
By Rogier W. Sanders, Ian A. Wilson and John P. Moore

Illustration by Patric Sandri

Rogier W. Sanders is a professor of virology at the Academic Medical Center at the University of Amsterdam and an affiliate faculty member at Weill Cornell Medicine in New York City. His research focuses on the design of novel vaccines against HIV.

Ian A. Wilson is a professor in and chair of the department of integrative structural and computational biology at the Scripps Research Institute. His current research involves precisely modeling the physical interactions between the immune system and certain viruses, particularly HIV, influenza and hepatitis C.

John P. Moore, who has conducted research on HIV vaccines since 1988, is a professor of microbiology at Weill Cornell Medicine.



MORE THAN 30 YEARS AFTER SCIENTISTS IDENTIFIED HIV AS THE CAUSE OF AIDS, we still have not managed to devise an effective vaccine against the virus. An array of drugs can usually keep the infection under control for decades, but a vaccine that prevents infection in the first place would be the best weapon—particularly in the developing world, where the costs of drugs and other factors can put effective therapy beyond the reach of many. Without treatment, HIV infection usually runs silently and progresses to severe immunodeficiency (AIDS) and death over the course of several years.

The long delay in developing a vaccine is not for want of trying or even a lack of funding. The problem is that HIV is like no other virus scientists have ever tackled. For any antiviral vaccine to work, it has to arouse the immune system to attack and destroy the virus of concern before it can invade cells and spread through the body. But HIV has evolved many defenses against the human immune system. Devilishly, it kills or impairs critical immune cells that are supposed to coordinate the body's response against it. And it is an unparalleled master of disguise that has so far thwarted the efforts of vaccine makers to teach the body how to quickly recognize and block its many variants from infecting humans.

The three of us and our colleagues have recently managed, after nearly two decades of trying, to create a synthetic protein that should help overcome the difficulties vaccine makers have faced in the past. We have shown that this molecule can elicit a strong response to HIV in animals. To serve as the basis for a vaccine in people, it will need to be modified to become more powerful and able to prevent infection by a much broader range of viral strains. That work will take time. But our laboratory and many others are already pursuing the remaining challenges and are optimistic that we are on the right course at last.

THE VISION

THE PROTEIN we constructed mimics the viral protein called envelope, or Env, more completely than has ever been possible. Env rises from the surface of HIV like a spike and enables the virus to enter immune system cells known as CD4+ T lymphocytes. These T cells normally communicate with other parts of the immune system through various proteins—including two called CD4 and CCR5—that dot their outer surface like signaling towers on a fortress wall. As HIV attempts to enter the immune cells, one of its envelope proteins first latches onto the CD4 protein, which allows it to then bind to CCR5 as well. Next the envelope protein twists and rearranges itself so that the outer membranes of the virus and the immune cell fuse together. As the membranes fuse, the virus releases its genes into the cell, which produces billions of copies of the virus; these viral particles in turn break out of the cell and spread to other cells, where the infective process repeats.

Researchers have long dreamed of preventing HIV infection by blocking the envelope protein's maneuvers. The most logical approach would be to "teach" the body's immune system to produce molecules called antibodies that would specifically recognize and adhere to the envelope protein on HIV. In theory, such

IN BRIEF

Although the medical community has made a lot of progress in treating infection with HIV, it has not developed a vaccine that is both safe and broadly effective.

Part of the problem is that the viral protein best suited to serve as the basis for a vaccine against HIV falls apart as soon as researchers try to manipulate it in any way.

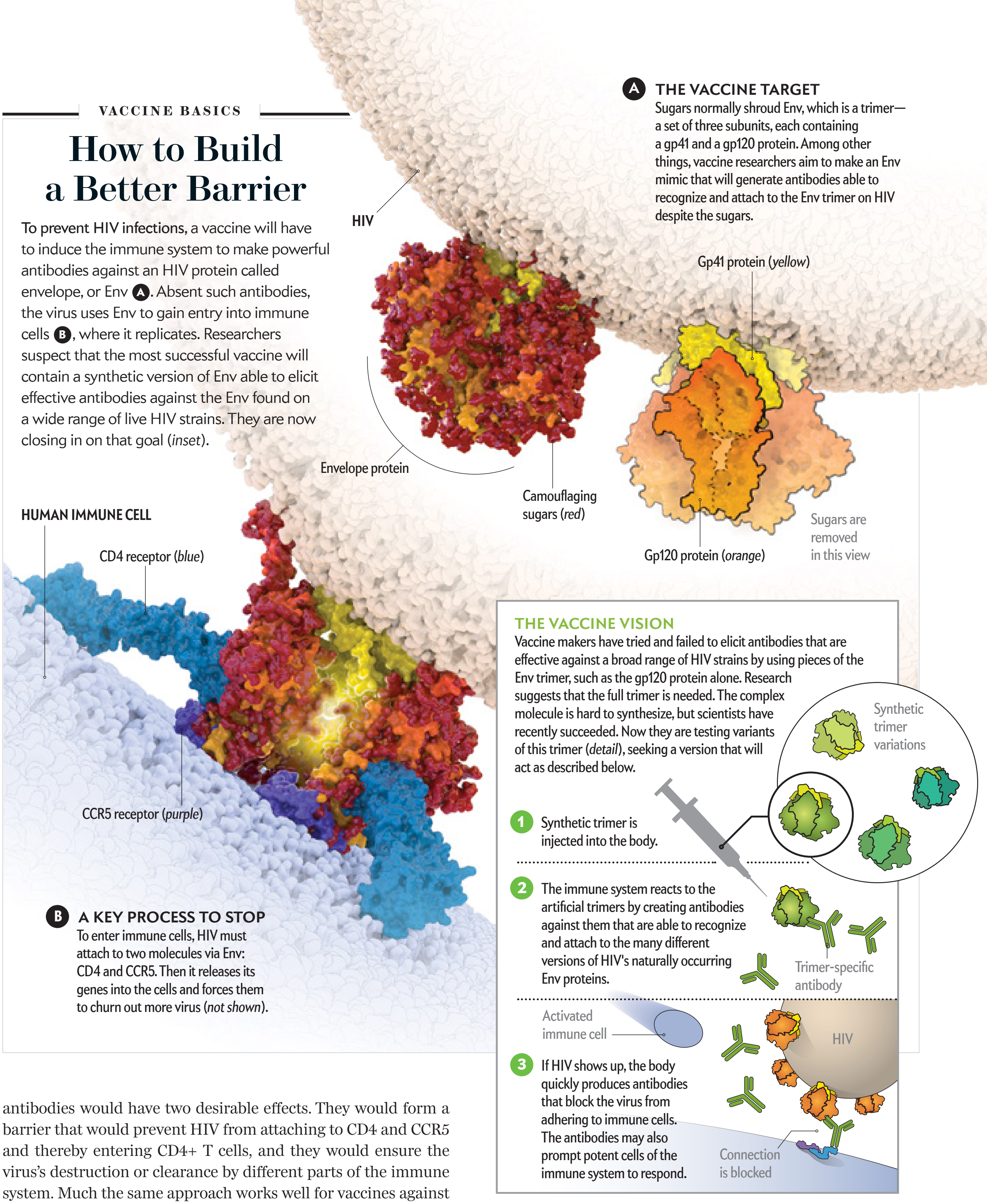
Unfortunately, these broken bits of protein do not, by themselves, provoke the immune system to create protective antibodies that can stop the virus from entering human cells.

After almost two decades of work, the authors created a synthetic protein that does not disintegrate and that mimics HIV proteins well enough to raise desirable antibodies in animals. The protein, or ones like it, must be further refined to yield an effective vaccine.

VACCINE BASICS

How to Build a Better Barrier

To prevent HIV infections, a vaccine will have to induce the immune system to make powerful antibodies against an HIV protein called envelope, or Env (A). Absent such antibodies, the virus uses Env to gain entry into immune cells (B), where it replicates. Researchers suspect that the most successful vaccine will contain a synthetic version of Env able to elicit effective antibodies against the Env found on a wide range of live HIV strains. They are now closing in on that goal (*inset*).



antibodies would have two desirable effects. They would form a barrier that would prevent HIV from attaching to CD4 and CCR5 and thereby entering CD4+ T cells, and they would ensure the virus's destruction or clearance by different parts of the immune system. Much the same approach works well for vaccines against other viruses, such as hepatitis B: a protein from the pathogen's surface is produced in the lab through genetic engineering; when injected into a person, such proteins cannot themselves cause disease (because the rest of the virus is absent), but they can induce the immune system to raise antibodies that will home in on and destroy any invading virus that displays the same or similar proteins.

Unfortunately, HIV thwarts the standard approach to developing vaccines because its envelope proteins have a nasty habit of falling apart as soon as they are separated from an intact virus. These pieces include the gp120 subunit (the part of the envelope protein that attaches to CD4) and the gp41 subunit, which anchors the envelope protein in the viral membrane and later

Illustration by Falconieri Visuals (main image) and Jen Christiansen (vaccine schematic) facilitates the fusion of the viral and immune cell membranes.

Now you might think that the envelope protein's tendency to fall apart would not be too much of a problem. After all, the virus cannot infect a cell without gp120 attaching itself to the CD4 signaling protein, and the immune system can and does make antibodies against individual gp120 molecules. Indeed, for years researchers tried without success to make a vaccine using gp120 subunits (and some are still trying). It turns out that antibodies made against single gp120 proteins do not trigger a strong immune response against the virus that infects people. Studies of whole Env proteins, in contrast, suggest that antibodies against them are much more effective at targeting HIV for destruction.

Finally, in 1998, one of us (Moore) decided that producing a successful vaccine would probably require abandoning the gp120 route and focusing on making a vaccine based on the full envelope protein. Creating such a vaccine would be hard for many reasons, not the least of which is that each envelope protein is complex: it is a trimer, consisting of three copies of gp120 and gp41 components. Another of us (Sanders) joined the effort a short time later, followed, soon after, by our other co-author (Wilson).

We have created a working first-generation prototype of a protein that can be modified to induce the most effective antibodies against HIV.

MULTIPLE CHALLENGES

TO PREVENT HIV infections, any vaccine—including one based on our research—will have to meet many challenges. For one thing, it will have to spur the immune system to produce particular kinds of antibodies. The most effective antibodies are those that both recognize an intact virus (in the case of HIV, specifically by homing in on the envelope protein) and that bind to it in such a way that they prevent that virus from entering a cell. Researchers call these crucial defense molecules neutralizing antibodies because they neutralize the infectivity of the virus.

To prevent infection around the world, however, we cannot raise just any old neutralizing antibodies; we need ones that are "broadly active": able to recognize many different variants of envelope proteins and to stop them from using CD4 and CCR5 to enter immune cells. The ideal neutralizing antibodies would presumably home to parts of the envelope protein that do not differ much among viral strains. Generating broadly active neutralizing antibodies against several different parts of Env might, if possible, be an even better strategy.

Researchers also want the antibodies raised by a vaccine to react to the envelope protein even though it is shrouded in an extraordinarily thick blanket of sugars that essentially mask HIV from the immune system. In the course of untreated HIV infections, the immune system manages to mount a response (including making neutralizing antibodies) that limits viral replication for years, but that response is too slow and weak to eradicate HIV fully. And it can take months or years for the body to figure out how to make neutralizing antibodies that bypass or recognize HIV's camouflaging sugars. In the meantime, the virus destroys more and more immune cells that the body can ill afford to lose.

TRIAL AND ERROR

MAKING A TRIMER that met two of our key criteria—that it would not disintegrate and would trigger neutralizing antibodies against the relevant strains of HIV—took our team multiple attempts (all funded by the National Institutes of Health) and the better part of two decades to accomplish.

We began by isolating *Env* genes from a particular strain of HIV and using them to synthesize Env proteins. To do this, we eliminated the part that normally anchors the envelope protein to the HIV surface. Our first attempt resulted in a protein that still fell apart. Several other groups of scientists tried to get around the problem by genetically engineering the envelope protein in a way that practically guaranteed the components would stay together. Sure enough, the resulting molecules did not completely fall apart, but their structure was so different from that of the envelope proteins that are found on HIV that they proved incapable of eliciting the necessary antibodies.

It was time to look for clues in other viruses that had some structural similarities to HIV. We realized that the surface proteins on some of them had a kind of chemical strut that linked their equivalent of the gp120 and gp41 proteins with a pair of sulfur atoms. We started looking for places where we could add such sulfur struts to the HIV envelope proteins that we were synthesizing and used what was already known about how the gp120 and gp41 components of the HIV trimer fitted together to make some educated guesses about where to place the sulfur struts to link everything together more strongly. By trial and error, we found the right locations, but the resulting trimer still crumbled—just in a different way than our previous attempts.

We then made a minor tweak to the gp41 component. All proteins are made up of various amino acids, whose electrical charges, among other things, cause the proteins to adopt distinctive shapes. Sanders decided to force the gp41 portion of our artificial trimer to adopt slightly different shapes by making particular amino acid substitutions. Eventually he found one alternative composition (replacing an isoleucine with a proline) that allowed the trimer to stay together. We gave our engineered protein the name "SOSIP" in honor of the two gambits that had made it possible: the first three letters (SOS) refer to the sulfur struts, and the last two (IP) indicate the key tweak we made in the gp41 protein.

And there things stood for many years. Our trimers were stable, but when we put them in a liquid, as would be needed for a vaccine, they just clumped together, making them useless.

Two critical developments finally enabled us to make new progress. First, Andrew Ward of the Scripps Research Institute, then an assistant professor, joined the effort to determine the physical structure of the Env trimer. Ward made highly detailed photographs of our SOSIP trimers with an electron microscope and showed that they were attracting fatty globules, or lipids, that basically made the trimers very sticky, causing them to congeal like chewing gum. And whereas some of our artificial trimers looked like viral envelope proteins, others had adopted very odd shapes indeed. Clearly, we were not consistently making the kinds of spike-mimicking trimers we were after.

Guided by the electron micrographs, we figured out a way to chop off a section at the end of our engineered trimers that was absorbing the meddlesome lipid molecules. We called these truncated trimers SOSIP.664 because of where we now cut them off: each third of the trimer consists of a long chain of amino acids, and we cut them off at the 664th amino acid in the chain. Looking at these slightly shorter trimers through the electron microscope, Ward saw that they all closely resembled the visible part of the spiky structures found on infectious HIV strains.

At this point, SOSIP.664 had the amino acid composition of the envelope protein from one variant of one strain of HIV, but we wanted to construct a trimer that was most likely to elicit production of neutralizing antibodies that had broad activity against many strains.

No one really knows, even now, exactly how to make a trimer that will induce broadly neutralizing antibodies in people. But our best chance of doing so is to make sure, at a minimum, that the trimer can be recognized—that is bound—in lab tests with a collection of broadly neutralizing antibodies that have been gathered from some people infected for many years with different strains of HIV. In other words, for existing broadly neutralizing antibodies to attach to a particular trimer at all, it must appear pretty similar—from a biochemical point of view—to naturally occurring Env proteins. And thus, injecting such a closely matched trimer into uninfected humans might well prompt the immune system to produce similarly powerful antibodies.

Because we could not predict which amino acid composition for the Env protein would give us the properties we wanted, we had no choice but to screen envelope proteins from about 100 different viral strains from patients around the world. We then made SOSIP proteins from all of them to find a variant that mimicked the spike under the electron microscope and could be bound in our lab tests by broadly neutralizing antibodies taken from people.

Eventually we found what we were looking for in samples collected from a six-week-old infant—given the code name BG505—who was born with HIV in Nairobi, Kenya. This particular viral strain was isolated by Julie Overbaugh of the Fred Hutchinson Cancer Research Center in Seattle and her colleagues at the University of Nairobi, and information about its genetic sequence—and thus the amino acid composition of its proteins—was passed to us for screening by the International AIDS Vaccine Initiative (IAVI).

The second development was the invention of a way to make a lot of this particular trimer, which we named BG505 SOSIP.664 (the BG505 trimer, for short), in as pure a form as possible. Among other things, this achievement allowed us to create crystals with the material through which we could shoot x-rays to determine its molecular structure. It also meant that we could make enough of it to test in animals and ultimately in people. Although lab tests of our trimers looked promising, we still needed to confirm the results in animals.

We injected the BG505 trimers into rabbits and monkeys and collected the antibodies against HIV that they made. When we added the antibodies to tissue cultures made up of human cells, we found that they did protect those cells against infection with the BG505 virus but not against other strains. Although the antibodies did not have the breadth of neutralizing activity that will in the end be needed, we had made a good start.

One of the next steps is to repeat these experiments in people. Much of our protein production research to date has been supported by the Bill & Melinda Gates Foundation and IAVI. We are also talking with IAVI and the NIH about designing and funding an exploratory clinical trial, which should enroll about 50 volunteers. We will not develop a protective vaccine right off the bat from this first artificial trimer—at least in its current configuration. Although results from lab animals are reasonably predictive of what happens in people, they are not foolproof. Clinical trials in people will teach us about how the human immune system responds to our artificial trimers. That kind of information, along with data from Wilson's lab on how closely the trimers resemble naturally occurring envelope proteins, should help us redesign our proteins to develop a protective vaccine. We will have to tweak what we create, probably more than once. We will also harness recent developments in understanding how the human immune system makes broadly neutralizing antibodies to improve how we deliver current and new trimers to people.

In essence, we have created a working first-generation prototype that we can modify in different ways to determine which configuration will be most likely to produce the most effective antibodies. Our ultimate goal—manufacturing a vaccine that induces broadly neutralizing antibodies against the most common strains of HIV in people—is still far from assured. But the good results that we have achieved so far with our approach in animals and cell tests suggest that the problem is not unsolvable.

And now the research community has the SOSIP tool kit and the methods to help create the best proteins possible for use as a vaccine. Many different groups are currently making their own versions of these spike-mimetic trimers to test their various vaccine designs. The coming years should finally be productive ones for a field that has been battering away at this tough, tough problem for a long, long time. SA

MORE TO EXPLORE

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FROM OUR ARCHIVES

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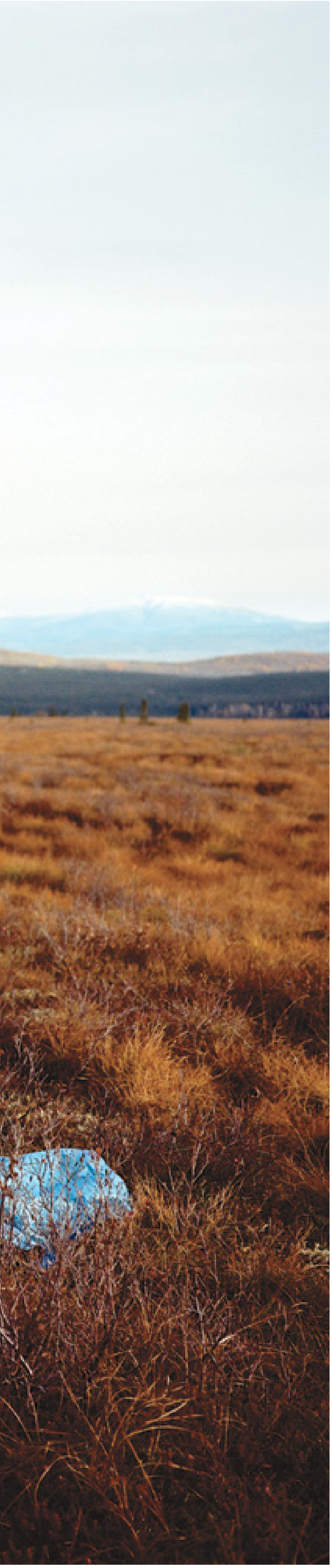
SCIENTISTS drill out a meter-long core of permafrost soil at the Eight Mile Lake research site near Healy, Alaska, in September. The dark color and texture (*opposite page*) indicate the soil is packed with organic matter that can decompose and give off greenhouse gases.



CLIMATE CHANGE

THE PERMAFROST PREDICTION

Thawing Arctic tundra will likely speed up climate change for a century or more. The question is: How drastically?

By Ted Schuur

IN BRIEF

Permafrost—soil frozen year-round—is thawing widely across the Arctic. Microbes are breaking down plant and animal remains in the warming soil, releasing carbon dioxide and methane to the atmosphere.

The Northern Hemisphere permafrost region is vast and contains about 1,450 billion metric tons of organic carbon, almost twice as much carbon as exists in Earth's atmosphere.

Data from numerous sensors suggest that 5 to 15 percent of that carbon could escape this century. At 10 percent, 130 billion to 160 billion metric tons of carbon would enter the atmosphere, accelerating global warming. Slowing overall warming is the best way to prevent permafrost from heating up.

Photographs by Brian Adams

Ted Schuur is a professor of ecosystem ecology at Northern Arizona University. He has conducted almost two decades of field research across the Arctic. He is also the lead investigator for the Permafrost Carbon Network, an international consortium of researchers that synthesizes new findings about permafrost carbon and climate.

THE SOLID, 20-KILOGRAM BLOCK OF HARDENED snow and ice somehow slides free from my rubber-gloved grasp and drops back down into the long ditch I am excavating in deep snow, landing with a crunch. On my knees at the edge of the trench, I straighten up to catch my breath and arch my sore lower back, protected with a weight-lifting belt. On this bright, cold day in interior Alaska, five scientists and I are digging out tons of snow along the fourth of six snow fences positioned on a gradual hill on the tundra, hauling it away on sleds. Our labor is part of an experiment designed to warm the ground, simulating what future climate may do in this remote location just outside of Denali National Park.

It is early April, and my team is spending more than a week removing compressed snowdrifts that have accumulated along the fences we install every fall at the site. Each fence is about one and a half meters high and eight meters long. The extra snow insulates the ground from the frigid winter air like a blanket, keeping the surface of permafrost—soil that usually remains frozen year-round—warmer than it otherwise would be. We remove the excess snow so that spring's impact penetrates our experimental plots at the same time as the surrounding tundra region and so that no extra meltwater percolates down into the ground, altering the soil in comparison with that in the larger area.

Keeping the frozen soil warmer during winter causes it to thaw sooner and more extensively in the summer. This reaction is exactly what is projected to occur as temperatures rise across the Arctic and boreal ecosystems just south of the Arctic, which is happening twice as fast as the increasing global average. Permafrost contains rock, frozen soil and ice, so it thaws, rather than melts, when it warms. Like hamburger pulled from your freezer, it softens but does not become liquid. As permafrost thaws, previously frozen microbes reactivate and decompose the remnants of plants and animals accumulated into the frozen soil over hundreds to thousands of years, giving off carbon dioxide and methane.

The permafrost zone that circles the northern part of Earth holds so much organic material in soils that releasing just a fraction of it as greenhouse gases into the atmosphere would dramatically raise the rate of global warming. Our experiment in Alaska is one important part of integrated research around the world to figure out how big this effect is likely to be over the coming decades. We are now starting to know enough to make solid predictions.

VAST QUANTITIES COULD THAW

HOW CAN WE POSSIBLY put a number on how much permafrost will thaw, and how fast, and how much the carbon release will affect global warming? A quantification would have to assess a massive area of the planet. The permafrost zone extends across 16.7 million square kilometers of the Northern Hemisphere, almost one quarter of the ice-free land area. And the frozen ground can be tens to hundreds of meters deep. (Much of the Southern Hemisphere's high latitudes is covered by ocean or ice sheets on land, so permafrost extent there is limited.)

Although satellites and remote-sensing equipment can accurately record changes in ice sheets such as those on Greenland, there is no comprehensive remote-sensing system for permafrost regions. For years scientists monitored ground sensors installed in certain permafrost spots, but we just did not have enough data points worldwide. We have steadily added more sensors, however. The Global Terrestrial Network for Permafrost now tracks more than 1,000 boreholes lined with instruments that monitor temperatures in the top few meters of soil as well as deeper underground.

The network has shown that permafrost has been warming

1

2

SENSORS in white chambers near the snow-capped Alaska Range measure the soil's uptake and release of carbon dioxide (*1*). Researcher Meghan Taylor of Northern Arizona University records the data (*2*).

steadily over the past several decades, setting new records in 2014 and 2015 at many locations. The most dramatic increases have occurred where soil temperatures have historically been very cold, from –10 to –5 degrees Celsius. We have also seen increases in temperature in permafrost that is closer to the freezing point, from –2 to zero degrees C, where a one-degree change can have a big impact. In some locations where permafrost is just below the freezing point, the active layer—soil at the surface that thaws during summer and refreezes in winter—is becoming thicker. When we stitch together all these measurements worldwide, we get a good sense of soil-temperature change across the Arctic.

How much permafrost could thaw is only part of the calculation we want to make. We also need to know how much organic matter the softening soil contains. This past spring at the Eight Mile Lake research site, my team drilled down into the ground and pulled out cores of soil 1.5 meters deep, as we have done in various years since the project began more than a decade ago. Measurements by us and others across the tundra show that the top cubic meter of soil contains about 50 kilograms of organic carbon—carbon bound up in those partially decayed but frozen organisms (as opposed to inorganic carbon that is part of rock, unlikely to change regardless of temperature). That amount is about five times as much carbon as in nonpermafrost soils within the same region and about 100 times as much as is stored in shrubs and other plants that eke out a living in the Arctic.

Carbon can exist tens of meters down into the ground, too. Overall, researchers estimate that 1,330 billion to 1,580 billion metric tons of organic carbon is stored in Northern Hemisphere permafrost, almost twice as much carbon as exists in Earth's atmosphere. The top three meters of soil in the northern permafrost zone alone hold 50 percent as much carbon as the top three meters of soil everywhere else on the planet, even though the zone represents only 15 percent of the global soil area.

Scientists are also measuring organic carbon in places where we never have, such as permafrost that is submerged at the bottom of very shallow seafloors along parts of the Arctic coast. This permafrost is slowly degrading as seawater seeps into it, and we are not yet clear on how much organic carbon may be there. Carbon is also plentiful in thick sediments in vast Arctic river deltas, but we simply have not measured many sites. The best we can suggest at this point is that about 400 billion metric tons of additional carbon may be preserved in these disparate places.

HOW MUCH, HOW FAST?

GIVEN THE VAST STORES of organic carbon in permafrost, it seems plausible that thawing could release massive quantities of greenhouse gases. Pinning a number on that release depends on three key questions.

First, how much of the carbon might be converted into greenhouse gases? Microorganisms can easily metabolize and release some of the carbon but not all. As a result, some fraction of the carbon will simply remain in the ground because it is so inaccessible or inedible by microbes.

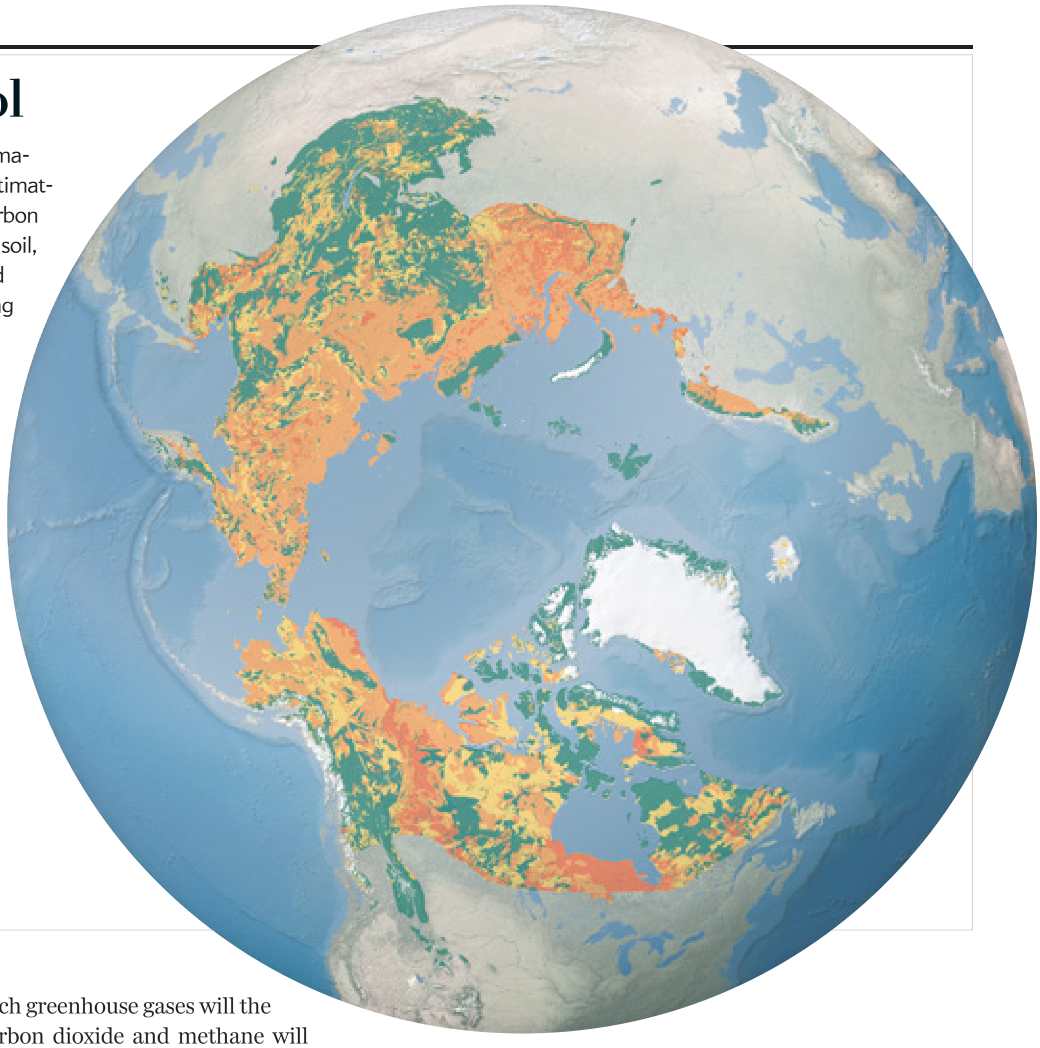
Second, how fast will microbial action release gases? Rapidly decomposing carbon can become airborne in less than a year after thaw, but more of the carbon will most likely be released gradually over decades after thaw, in part because it is already in a semidecomposed state that microbes only further degrade slowly.

Carbon Pool

The Northern Hemisphere's permafrost zone (*colors*) contains an estimated 1,035 billion metric tons of carbon in the top three meters of frozen soil, which could escape if the ground thaws, amplifying global warming significantly. Permafrost is nearly everywhere in the northernmost regions. It is more discontinuous further south, but many areas in both regions contain high carbon concentrations (*red* and *orange*).

Carbon in Top Three Meters of Soil (kilograms per square meter of surface area)

260
100
50
30
0.1



The third key question is: Which greenhouse gases will the microbes release? The mix of carbon dioxide and methane will determine the ultimate climate warming potential. Waterlogged, low-oxygen soils (known as anaerobic environments) such as peat bogs, for example, typically produce much more methane than carbon dioxide, and methane has about 33 times the global warming potential of carbon dioxide by weight over a century.

We track gas release at study sites such as Eight Mile Lake and the surrounding tundra with infrared gas analyzers that measure concentrations in the air across seconds, days, seasons and years. The tundra at Eight Mile Lake appears to be losing more carbon to the atmosphere than it is absorbing. Warming the ground with snow along the fences helps plants grow faster and larger, pulling and storing more carbon dioxide from the air. But it also helps microbes decompose more carbon in the soil. In the summertime, the extra plant growth completely offsets additional carbon release from the soil, but continued microbial activity throughout the long autumn and winter, when plants are dormant, shifts the annual balance to net carbon loss to the atmosphere.

When we combine our results with those from other types of experiments around the world, we conclude that thawing permafrost is spewing excess carbon into the atmosphere. Researchers bring data together through the Permafrost Carbon Network. Just like the parable of the blind men describing the elephant, field researchers across the Arctic each have important and unique information that when linked together creates knowledge about the true size and nature of this phenomenon. The Permafrost Carbon Network also synthesizes science results for reports, agency briefings and media interviews to inform decision makers and the wider public so these groups can decide how to respond to our changing Earth.

One recent synthesis project has helped answer the question about relative releases of carbon dioxide and methane. In aerobic conditions (dry soils), microbes mostly release carbon dioxide. But in anaerobic conditions in wetlands and peat soils, they release both carbon dioxide and methane. Christina Schädel, an assistant research professor at Northern Arizona University working with my group and a key player in the Permafrost Carbon Network, has been studying how this trade-off might ultimately affect climate.

In contrast to our field study, Schädel relied on experiments where frozen soil was taken into the laboratory and warmed in glass chambers so that the amount and rate of soil carbon converted into carbon dioxide or methane could be measured precisely. She used statistical techniques to bring data together from tests such as these around the world and has found that carbon dioxide is the predominant greenhouse gas by weight that is released by identical soil samples regardless of whether they were found in either aerobic or anaerobic conditions. Surprisingly, the climate impact of greenhouse gas release from aerobic decomposition is two times larger than for anaerobic de-

SOURCE: "CLIMATE CHANGE AND THE PERMAFROST CARBON FEEDBACK," BY E.A.G. SCHUUR ET AL., IN *NATURE*, VOL. 520; APRIL 9, 2015

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Map by Mapping Specialists

composition, despite the additional potency of methane, which is released only from the latter.

The implication is that permafrost thaw in relatively well-drained, upland soils most likely will have a greater impact on climate than a similar amount of thaw in lowland, waterlogged soils. Although methane is still a key part of the equation, the overall distribution of upland and lowland environments across the Arctic landscape will significantly determine permafrost thaw's impact on climate.

ACCELERATING CLIMATE CHANGE

BY SYNTHESIZING DATA from field sites and lab tests and combining that information with computer simulations of future climate scenarios, the Permafrost Carbon Network has generated an answer to the overarching question of how permafrost thaw might affect climate. In the expert judgment of its members, between 5 and 15 percent of the permafrost carbon pool is likely to be released this century, most of it as carbon dioxide.

The midrange—10 percent—of the carbon pool, as best we know it, means that 130 billion to 160 billion metric tons of additional carbon would enter the atmosphere. That amount, if released primarily in the form of carbon dioxide at a constant rate over a century, would be similar to the amount of carbon released worldwide thus far by deforestation and other land-use changes but much less than that from fossil-fuel emissions. Permafrost thaw will make climate change happen even faster than scientists project based on emissions from human activities alone. And permafrost carbon emissions are likely to continue beyond this century. Each additional ton of carbon released from the thawing Arctic into the atmosphere will impose additional costs on society.

Reducing permafrost thaw with some kind of local fixes across the Arctic is not a realistic option. The only real solution is to limit emissions from fossil fuels and from deforestation to slow global warming overall. That in turn will reduce emissions from Arctic thaw, giving communities at all latitudes more time to adapt.

Scientists have generated the 5 to 15 percent number for the first time only in the past year. We still do not have a comprehensive observation system in permafrost regions to make a firmer prediction. More sensors would allow us to better detect both slow and rapid change, which could be cause for either lessened or heightened concern. And they would help us detect important surprises that might arise.

New initiatives, such as the U.S. Department of Energy's Next-Generation Ecosystem Experiments–Arctic project and NASA's Arctic-Boreal Vulnerability Experiment, are helping to fill in important gaps in modeling and in scaling up site-based measurements such as those from Eight Mile Lake to the surrounding region and, ultimately, to the global scale.

One intriguing and critical question is whether extensive plant growth could counterbalance permafrost carbon release. The latest simulations tend to show that longer growing seasons, warmer temperatures, more plant nutrients released by decomposing soils, and natural shifts to faster-growing plants and trees might offset carbon release from permafrost during this century. But that assessment contradicts measurements from Eight Mile Lake and elsewhere, which show net carbon loss across an entire year.

Better simulation of how thawing ground subsides would also be useful; it is currently missing from large-scale models that simulate the permafrost carbon and climate interactions. As ice in permafrost melts and drains away, the ground subsides, which then causes permafrost to thaw more abruptly. Could widespread subsidence boost emissions forecasts even more?

My colleagues and I saw this very effect at Eight Mile Lake when we returned there this past spring. The boardwalks we had built almost a decade ago, along with the gas-flux monitors and other gear we had installed, had become twisted and angled from ongoing subsidence. The ground was undulating and pitted.

The spring 2016 thaw at Eight Mile Lake also went deeper than ever—more than a meter in some spots, an amount typically seen only at the end of summer in previous years. The unusual readings paralleled similar extremes elsewhere in the Arctic: record, early-season retreat of winter ice cover on the Arctic Ocean, early snowmelt across the Northern Hemisphere and early surface melt of the ice sheet in Greenland. Carbon emissions from permafrost are happening right now. The release of gases will not be a rapid burst that could alter climate abruptly, as some feared. But it will indeed be widespread and sustained over many decades, seriously compounding the daunting challenge that society already faces to slow global warming. SA

INSTRUMENT TOWER measures carbon dioxide and methane transfer between the air and soil year-round, indicating whether the ecosystem experiences a net gain or loss of gases annually.

MORE TO EXPLORE

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ANTHROPOLOGY

THE EVOLUTION OF MYTHS

Analyzing how stories change in the retelling down through the generations sheds light on the history of human migration going as far back as the Paleolithic period

By Julien d'Huy

Illustration by Jon Foster

Julien d'Huy is a doctoral candidate in history at Pantheon-Sorbonne University in Paris. His multidisciplinary research, conducted in association with the Institute of African Worlds, draws on evolutionary theory and computer modeling in the comparative analysis of myths.

THE GREEK VERSION OF A FAMILIAR MYTH STARTS WITH ARTEMIS, GODDESS OF THE HUNT and fierce protectress of innocent young women. Artemis demands that Callisto, "the most beautiful," and her other handmaidens take a vow of chastity. Zeus tricks Callisto into giving up her virginity, and she gives birth to a son, Arcas. Zeus' jealous wife, Hera, turns Callisto into a bear and banishes her to the mountains. Meanwhile Arcas grows up to become a hunter and one day happens on a bear that greets him with outstretched arms. Not recognizing his mother, he takes aim with his spear, but Zeus comes to the rescue. He transforms Callisto into the constellation Ursa Major, or "great bear," and places Arcas nearby as Ursa Minor, the "little bear."

As the Iroquois of the northeastern U.S. tell it, three hunters pursue a bear; the blood of the wounded animal colors the leaves of the autumnal forest. The bear then climbs a mountain and leaps into the sky. The hunters and the animal become the constellation Ursa Major. Among the Chukchi, a Siberian people, the constellation Orion is a hunter who pursues a reindeer, Cassiopeia. Among the Finno-Ugric tribes of Siberia, the pursued animal is an elk and takes the form of Ursa Major.

Although the animals and the constellations may differ, the basic structure of the story does not. These sagas all belong to a family of myths known as the Cosmic Hunt that spread far and wide in Africa, Europe, Asia and the Americas among people who lived more than 15,000 years ago. Every version of the Cosmic Hunt shares a core story line—a man or an animal pursues or kills one or more animals, and the creatures are changed into constellations.

Folklorists, anthropologists, ethnologists and linguists have long puzzled over why complex mythical stories that surface in cultures widely separated in space and time are strikingly similar. In recent years a promising scientific approach to comparative mythology has emerged in which researchers apply conceptual tools that biologists use to decipher the evolution of living species. In the hands of those who analyze myths, the method, known as phylogenetic analysis, consists of connecting successive versions of a mythical story and constructing a family tree that traces the evolution of the myth over time.

My phylogenetic studies make use of the extra rigor of statistical and computer-modeling techniques from biology to elucidate how and why myths and folktales evolve. In addition to the Cosmic Hunt, I have analyzed other major families of myths that share recurring themes and plot elements. Pygmalion stories depict a man who creates a sculpture and falls in love with it. In Polyphemus myths, a man gets trapped in the cave of a monster and escapes by insinuating himself into a herd of animals, under the monster's watchful eye.

This research provides compelling new evidence that myths and folktales follow the movement of people around the globe. It reveals that certain tales probably date back to the Paleolithic period, when humans developed primitive stone tools, and spread together with early waves of migration out of Africa. My phylogenetic studies also offer insights into the origins of these myths by linking oral stories and legends passed down from generation to generation to motifs that appear in Paleolithic rock art images. Ultimately I hope my ongoing quest to identify prehistoric protomyths may even offer a glimpse of the mental universe of our ancestors when *Homo sapiens* was not the only human species on Earth.

TRAIL OF THE COSMIC HUNT

CARL JUNG, THE FOUNDING FATHER of analytic psychology, believed that myths appear in similar forms in different cultures because they emerge from an area of the mind called the collective

IN BRIEF

Scholars have long wondered why complex mythical stories that surface in cultures widely separated in space and time are strikingly similar.

New research models harness conceptual and statistical tools from evolutionary biology to untangle the history of myths.

Phylogenetic trees reveal that species of myths evolve slowly and parallel patterns of mass human migration out of Africa and around the globe.

Recent studies provide insights into the prehistoric origins of some myths and the migration of Eurasians to North America more than 15,000 years ago.

unconscious. "Myths are first and foremost psychic phenomena that reveal the nature of the soul," Jung argued. But the dissemination of Cosmic Hunt stories around the world cannot be explained by a universal psychic structure. If that were the case, Cosmic Hunt stories would pop up everywhere. Instead they are nearly absent in Indonesia and New Guinea and very rare in Australia but present on both sides of the Bering Strait, which geologic and archaeological evidence indicates was above water between 28,000 and 13,000 B.C. The most credible working hypothesis is that Eurasian ancestors of the first Americans brought the family of myths with them.

To test this hypothesis, I created a phylogenetic model. Biologists use phylogenetic analysis to investigate the evolutionary relationships between species, constructing branching diagrams, or "trees," that represent relationships of common ancestry based on shared traits. Mythical stories are excellent targets for such analysis because, like biological species, they evolve gradually, with new parts of a core story added and others lost over time as it spreads from region to region.

In 2012 I constructed a skeletal model based on 18 versions of the Cosmic Hunt myth previously collected and published by folklorists and anthropologists. I converted each of those accounts of the myth into discrete story elements, or "mythemes"—a term borrowed from the late French structural anthropologist Claude Lévi-Strauss. Like genes, mythemes are heritable characteristics of "species" of stories, which pass from one generation to the next and change slowly. Examples of Cosmic Hunt mythemes include: a woman breaks a taboo; a divine person stops a hunter; a god transforms an animal into a constellation. My initial analysis yielded a database of 44 mythemes. For each version of a story, I then coded mythemes as either 1 (present) or 0 (absent) and applied a successive series of statistical algorithms to trace evolutionary patterns and establish family trees. In 2013 I expanded the model to include 47 versions of the story and 93 mythemes. Eventually I used three separate databases to apply different algorithms and cross-check my results.

One of the most up-to-date phylogenetic trees of the Cosmic Hunt [*see box on page 68*] suggests that the family of myths arrived in the Americas at several different points. One branch of the tree connects Greek and Algonquin versions of the myth. Another branch indicates passage through the Bering Strait, which then continued into Eskimo country and to the northeastern Americas, possibly in two different waves. Other branches suggest that some versions of the myth spread later than the others from Asia toward Africa and the Americas.

A MYTHICAL METAMORPHOSIS

EVOLUTIONARY BIOLOGISTS HAVE observed that most species do not change much for the greater part of their histories. When significant evolutionary change occurs, it is generally restricted to rare and very fast events of branching speciation. This phenomenon is called punctuated equilibrium. The same appears to hold true with myths. When sister mythological versions diverge rapidly because of migration bottlenecks, challenges from rival populations, or new environmental and cultural inputs, those events are followed by extended periods of stability.

By and large, structures of mythical stories, which sometimes remain unchanged for thousands of years, closely parallel the history of large-scale human migratory movements. Ironically, phylogenetic analysis reveals that one of the most enchanting mythical stories of sudden transformation—the Pygmalion story—is a prime example of this stable pattern of evolution.

As the Greeks tell it, Pygmalion, a handsome sculptor from Cyprus, spurns the company of local women relegated to a life of loveless prostitution for failing to pay proper homage to Aphrodite, the goddess of love and patron deity of the island. Throwing himself into his work, Pygmalion chisels an ivory statue of a woman, which he names "Galatea" (or "sleeping love"). He dresses the sculpture in fancy clothes and jewels, kisses and caresses it, and talks to it every day. During a festival in honor of Aphrodite, Pygmalion goes to the goddess's temple, sacrifices a bull and prays for a wife just like his beloved statue. When he returns home and kisses Galatea, he is surprised by the statue's warmth. Aphrodite has brought Galatea to life.

Roman poet Ovid immortalized the Greek folktale in *Metamorphoses* and inspired countless writers, dramatists and artists ever since.

My research suggests the evolution of the Pygmalion myth followed a human migration from northeastern to southern Africa that previous genetic studies indicate took place around 2,000 years ago. In folktales told by various tribes along that route, a man carves an image of a woman and falls in love with it; the doll comes to life and marries the master. According to the Venda of South Africa, a man sculpts a woman out of wood. After she is animated, the head of the tribe tries to kidnap her. The sculptor resists and throws the woman to the ground, whereupon she turns back into wood.

A phylogenetic tree I constructed using the Greek version of Pygmalion and a version from the Bara people of Madagascar as starting points yielded intriguing results. The Greek and Bara myths mirror each other structurally, even though they represent the greatest geographical separation of any of the stories included in the computer model. In addition, the Bara settled on an island that did not allow for great population expansion and mythological diversification, and the Greeks remained isolated for much of their history from exposure to African folktales. Nevertheless, both the Bara and Greek versions of the myth bear remarkable similarities to an earlier version of the story from the Berber tribes of the Sahara.

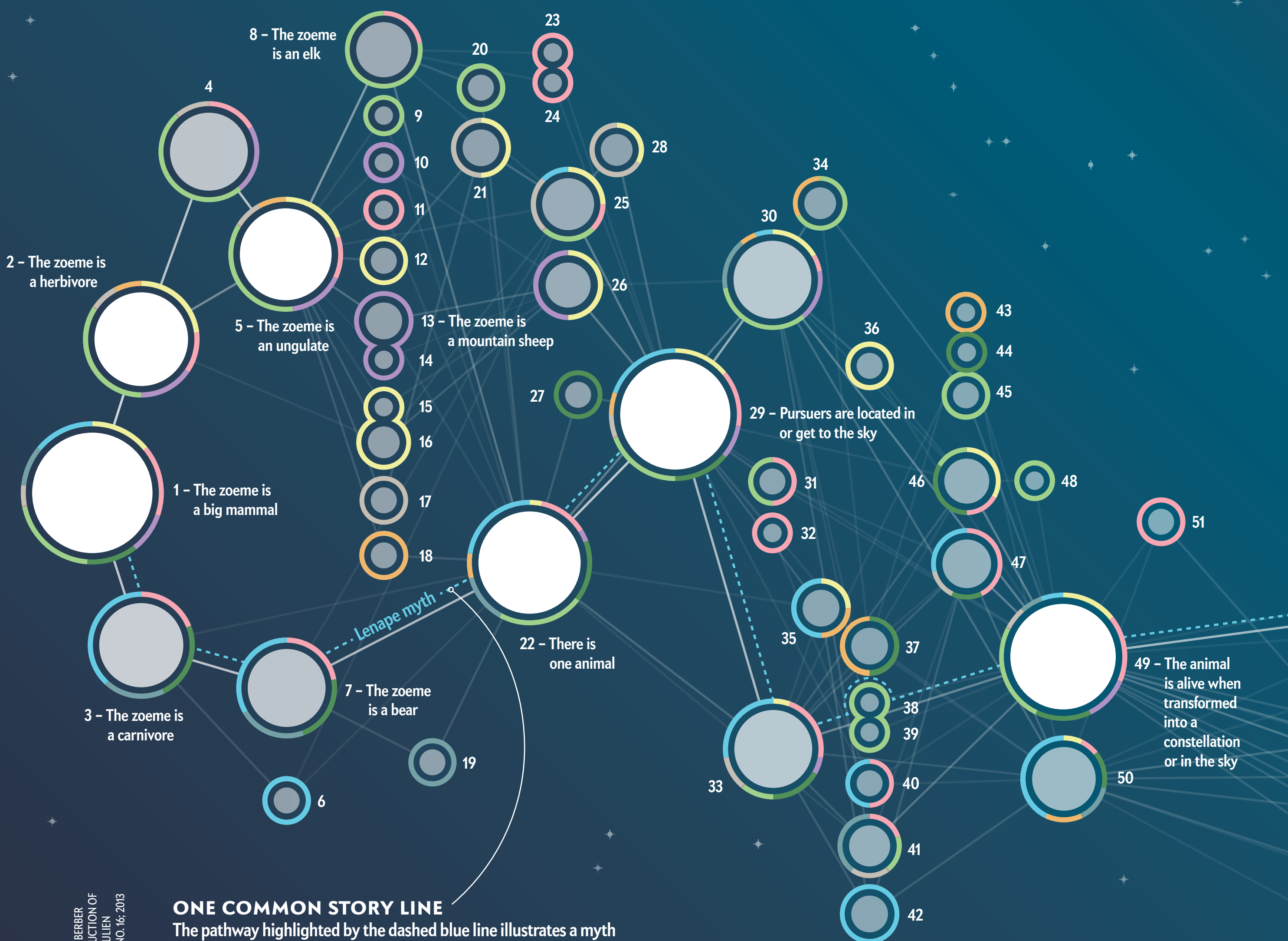
Statistical and empirical analysis suggests that the accounts of the Greeks and Baras probably preserve a version of the Pygmalion saga that originated with the Berbers between 3,000 and 4,000 years ago and appears to encapsulate a very ancient version of the myth: A man makes a statue from a tree trunk to lessen his solitude; he or another man clothes it; the statue comes to life, thanks to a god, and turns into a beautiful young lady; she becomes the wife of her creator, even though another person also desires to marry her. Of course, the real protomyth was probably as rich in complexity as the versions on which the reconstruction is based.

THE MONSTER IN THE CAVE

IN THE PAST, COMPARATIVE MYTHOLOGY scholars relied heavily on intuition and manual processing of information, which limited both the breadth and granular detail of the work they could do. With computer-aided phylogenetic analysis, we can now test the impact of mythological borrowings between different cultural groups. We can create large and flexible databases that in-

Deconstructing Myths

Cosmic Hunt myths, which depict constellations of stars as animals pursued by hunters, are common in Eurasia and the Americas. Comparative mythologists study the surprising similarities and subtle variations in the myths of widely dispersed cultures using analytic tools developed by evolutionary biologists. First, they break down a particular "species" of mythical stories into small building blocks that are analogous to genes: "mythemes." Then they record such factors as the frequency of the elements in various stories (*below*). Computer analyses of similar elements can reveal which versions came earliest and how the core stories changed with time and place. The mythemes depicted here are the building blocks of various Cosmic Hunt stories related to Ursa Major, Ursa Minor, Orion and the Pleiades.



ONE COMMON STORY LINE

The pathway highlighted by the dashed blue line illustrates a myth from the Lenape Indians of the northeastern U.S. about how the Ursa Major constellation took the shape of a bear. The Lenape legend shares several mythemes with various Cosmic Hunt myths preserved by other cultural groups in Eurasia and the Americas, including: The zoeme is a big mammal (*1*); pursuers are located in or get to the sky (*29*); the animal is alive when transformed into a constellation (*49*); one of the main constellations of the story is the Big Dipper (*86*).

SOURCE: "A COSMIC HUNT IN THE BERBER SKY: A PHYLOGENETIC RECONSTRUCTION OF PALAEOLITHIC MYTHOLOGY," BY JULIEN D'HUY, IN *LES CAHIERS DE L'AARS*, NO. 16; 2013

Graphic by Accurat

HOW TO READ THIS FIGURE

Each of the 88 circles in the illustration represents a Cosmic Hunt mytheme (story component) as defined by the author. Below, we have loosely ordered those mythemes (*listed more fully at right*) according to general categories, including zoemes (animals) (□), pursuit details (╲), transformations of animals and pursuers (○), and manifestations of the stories in particular constellations (+).

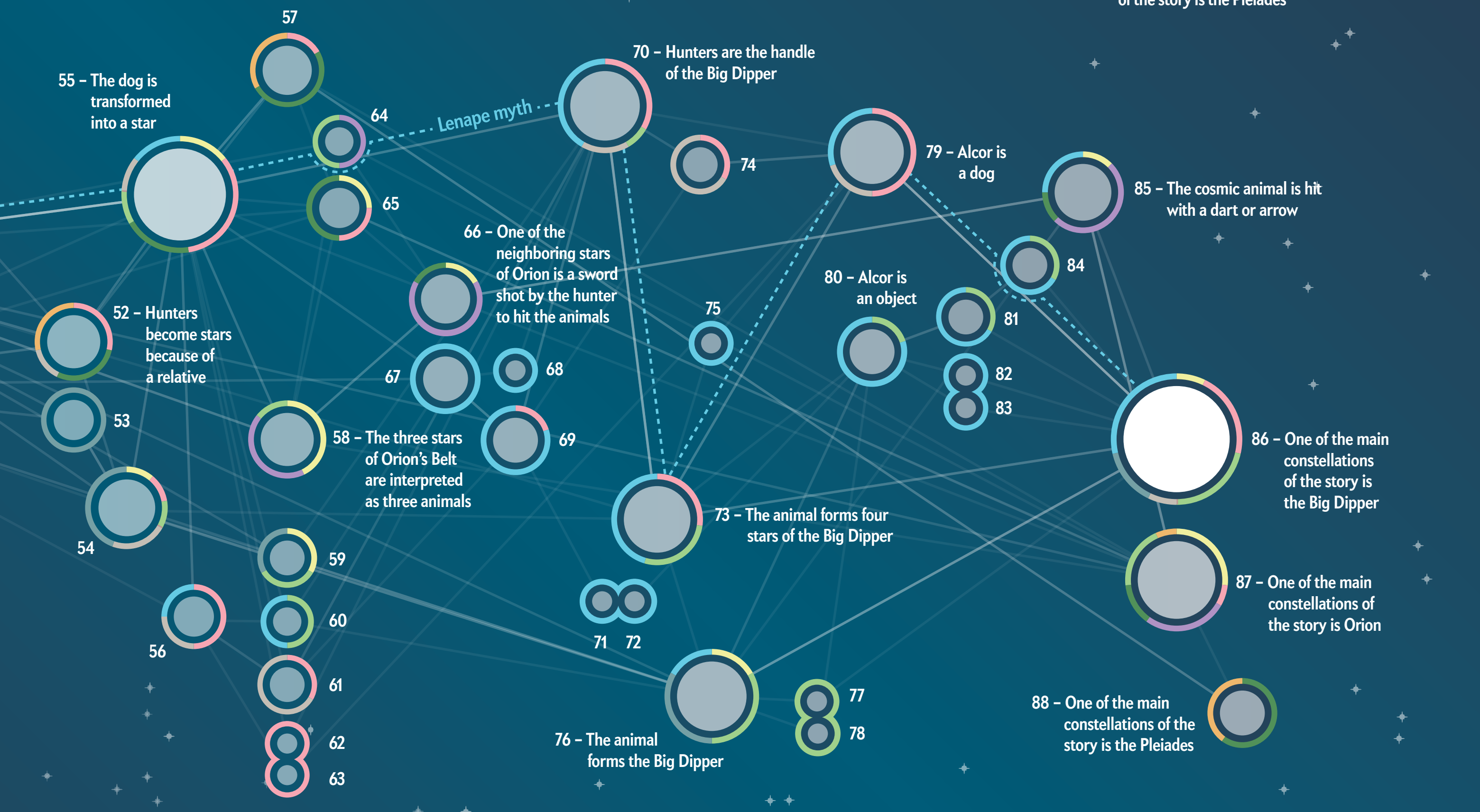
Circle size and opacity show how many tales the mytheme appears in, ranging from 1 to 43.

Lines connect mythemes that occur in tales together.

Ring color indicates the regions associated with each mytheme's tale. For example, this mytheme occurs in three tales, one from Guiana (*orange*) and two from Asia (*light green*).

- Africa
- American Coast-Plateau/British Columbia
- American Great Basin/Great Southwest
- Northeastern America
- Asia
- Arctic
- Basque
- Greece
- Guiana

□ 1 – The zoeme is a big mammal
□ 2 – The zoeme is a herbivore
□ 3 – The zoeme is a carnivore
□ 4 – The zoeme is a horned animal
□ 5 – The zoeme is an ungulate
□ 6 – The zoeme is a fisher
□ 7 – The zoeme is a bear
□ 8 – The zoeme is an elk
□ 9 – The zoeme is a reindeer
□ 10 – The zoeme is a deer
□ 11 – The zoeme is a moose
□ 12 – The zoeme is a camel
□ 13 – The zoeme is a mountain sheep
□ 14 – The zoeme is an antelope
□ 15 – The zoeme is a zebra
□ 16 – The zoeme is a pig
□ 17 – The zoeme is an ox
□ 18 – The zoeme is a tapir
□ 19 – Zoeme is the pursuer's mother, who has been transformed into a bear
□ 20 – It is a six-legged animal
□ 21 – It is a domestic animal
□ 22 – There is one animal
□ 23 – There are four animals
□ 24 – There are seven animals
□ 25 – There are two animals
□ 26 – There are three animals
□ 27 – The Pleiades are an animal
□ 28 – Animals are associated with their owner
╲ 29 – Pursuers are located in or get to the sky
╲ 30 – There is one pursuer
╲ 31 – There are two pursuers
╲ 32 – There are five pursuers
╲ 33 – There are three, or at least three, pursuers
+ 34 – Orion is a pursuer
╲ 35 – There are seven pursuers
+ 36 – The sword of Orion is a pursuer
╲ 37 – A woman breaks a taboo
╲ 38 – The zoeme captures the sun
╲ 39 – An animal is punished for its pride
╲ 40 – A man goes down alone from the sky to Earth and destroys the way to access to the sky
╲ 41 – A divine person stops a hunter
╲ 42 – The hunt continues until the fall
+ 43 – The Hyades are a game
+ 44 – Betelgeuse is a game
+ 45 – Cassiopeia is a game
╲ 46 – Pursuers are dogs
╲ 47 – Pursuers are members of the same family
╲ 48 – An animal pursues an animal that pursues an animal
○ 49 – The animal is alive when transformed into a constellation or in the sky
○ 50 – The animal is dead when transformed into constellation
○ 51 – A man turns his brothers into stars
○ 52 – Hunters become stars because of a relative
○ 53 – A god transforms a nymph into a bear
○ 54 – A god transforms an animal into a constellation
○ 55 – The dog is transformed into a star
+ 56 – Each animal is transformed into a star of the Big Dipper
+ 57 – The Pleiades are hunters
+ 58 – The three stars of Orion's Belt are interpreted as three animals
+ 59 – Members of the same family turn into Ursa Major and Ursa Minor
+ 60 – One animal turns into a star of the Big Dipper
+ 61 – Two animals turn into two stars of the Big Dipper
+ 62 – Four animals turn into four stars of the Big Dipper
+ 63 – Seven animals form seven stars of the Big Dipper
+ 64 – Three stars of Orion's Belt are interpreted as one single animal
+ 65 – The three stars of Orion's Belt are interpreted as three pursuers
+ 66 – One of the neighboring stars of Orion is a sword shot by the hunter to hit the animals
○ 67 – The grease or the blood dripping from the animal's body falls on Earth and becomes something else
○ 68 – The grease becomes honeydew
○ 69 – The dripping blood of the animal tinges the autumn foliage
+ 70 – Hunters are the handle of the Big Dipper
○ 71 – The grease becomes snow
+ 72 – Hunters form seven stars of the Big Dipper
+ 73 – The animal forms four stars of the Big Dipper
+ 74 – Hunters form five stars of the Big Dipper
+ 75 – Cutoff limbs are stars seen in winter
+ 76 – The animal forms the Big Dipper
+ 77 – The Big Dipper is a drawing
+ 78 – Three stars are the shadow of the animal
+ 79 – Alcor is a dog
+ 80 – Alcor is an object
+ 81 – Alcor is an arrow
+ 82 – Alcor is a knife
+ 83 – Alcor is a cooking pot
╲ 84 – The hero is the origin of warmth
╲ 85 – The cosmic animal is hit with a dart or arrow
+ 86 – One of the main constellations of the story is the Big Dipper
+ 87 – One of the main constellations of the story is Orion
+ 88 – One of the main constellations of the story is the Pleiades



corporate the wealth of empirical observations by scholars over the years. And we can expand those databases to include new versions of stories and test previous results.

In 2012 I constructed the initial model for a phylogenetic study of the Polyphemus myth based on 24 versions of the story from Europe and North America and 79 mythemes. Then I progressively enlarged the sample size to include 56 versions of the story and 190 mythemes drawn from a variety of previous studies published in English, French, German and Italian. I also created three separate databases and applied a variety of evolutionary and statistical algorithms to calibrate and cross-check my results.

Polyphemus, the monstrous one-eyed, human-eating progeny of Poseidon, god of the sea, makes a dramatic appearance in Homer's *Odyssey*. When Odysseus lands on the island of Cyclops in search of food, he and 12 men surreptitiously enter Polyphemus' cave. The giant returns from grazing his sheep, seals the entrance and devours four of Odysseus' men before leaving the next morning to tend his flock. That evening, after Polyphemus eats two more men, Odysseus gets him drunk on undiluted wine. Polyphemus asks his generous guest to tell him his name, and Odysseus replies, "Nobody." Once Polyphemus falls asleep, Odysseus blinds him with a sharpened stick hardened in a fire. Polyphemus screams for help, but when other Cyclopses arrive and ask who blinded him, he answers, "Nobody." Meanwhile Odysseus and his remaining men escape by clinging to the underbellies of the monster's sheep as Polyphemus lets them out to graze.

The Blackfoot Indians, an Algonquin tribe that depended on hunting buffalo to get enough food to survive, passed a related story from generation to generation. The trickster Crow, who is both human and bird, hides a herd of buffalo in a cave. Crow is eventually captured and placed over a smoke hole, which explains why, ever since, crows are black. Crow promises to free the buffalo. But he breaks his promise. Two heroic hunters transform themselves—one into a puppy, the other into a wood staff. Crow's daughter picks up the puppy and staff and takes them to the cave. There the two hunters transform themselves again, one into a large dog, the other into a man, to drive the buffalo aboveground. They get past Crow by hiding under the skin of a buffalo as the herd charges out of the cave.

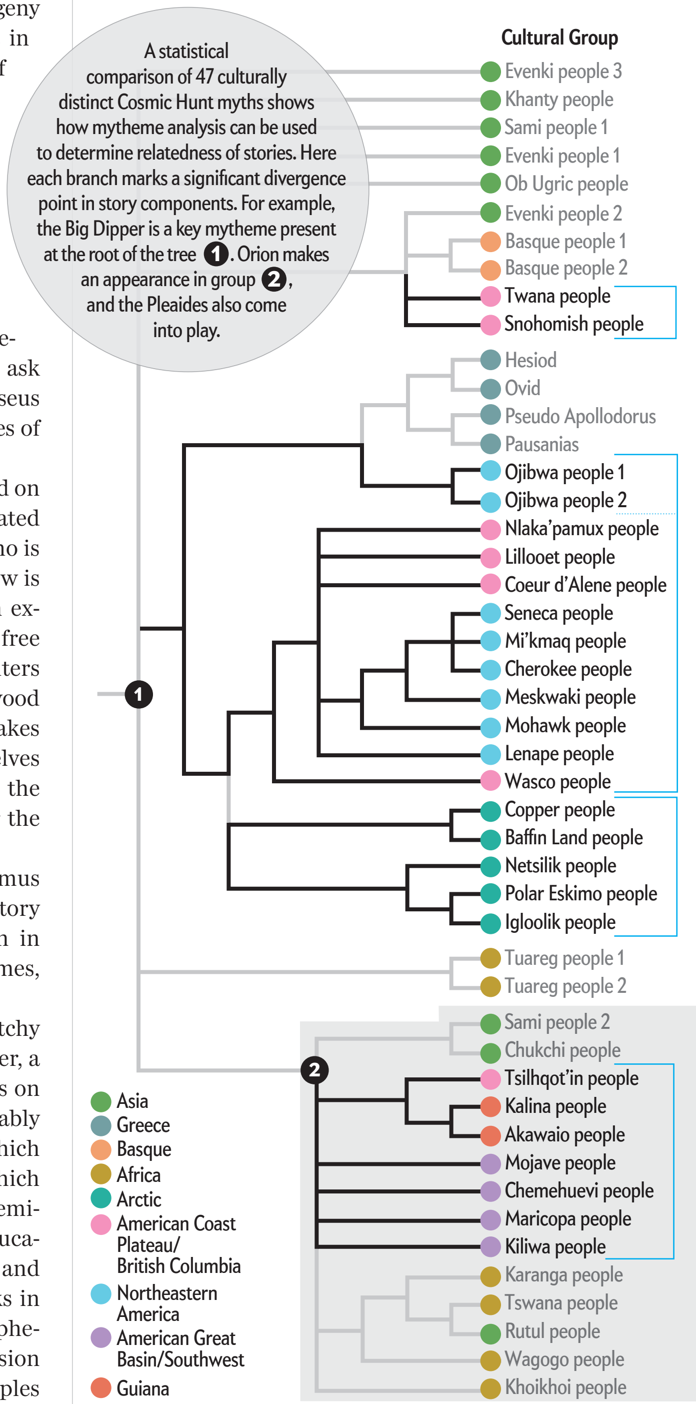
A composite phylogenetic tree of the family of Polyphemus myths indicates that the stories followed two major migratory patterns: The first, in Paleolithic times, spread the myth in Europe and North America. The second, in Neolithic times, paralleled the proliferation of livestock farming.

One version of the Polyphemus story, conserved in a sketchy form in Switzerland, may preserve an old form: The monster, a dwarf with one eye found by a hunter, is a master of beasts on a mountain. But this form of the story disappeared, probably as glaciers advanced during the Last Glacial Maximum, which peaked around 21,500 years ago. Then a new version, in which the monster resides in a shelter, appears to have been disseminated, thanks to successive migrations from areas in the Caucasus and Mediterranean that had provided refuge for people and other biological species from severe climate changes. Links in the phylogenetic tree suggest the Homeric versions of Polyphemus created an oral tradition with an independent diffusion among many groups, for instance, the ancestors of the peoples of modern-day Hungary and Lithuania.

GENEALOGY OF MYTHS

Family Tree

Analysis of variations in Cosmic Hunt myths using several different statistical models reveals that the humans who first populated the Americas brought the stories with them when they crossed the Bering Strait land bridge from Siberia more than 15,000 years ago. Branches in this model indicate how versions of the myth passed from generation to generation and to different cultural groups during four successive waves of migration.



SOURCE: JULIEN D'HUY

SCIENTIFIC AMERICAN ONLINE Listen to a podcast about the evolution of myths at ScientificAmerican.com/dec2016/myths

Graphic by Jen Christiansen

QUEST FOR ANCESTRAL PROTOMYTHS

PHYLOGENETIC RECONSTRUCTIONS of both the Polyphemus and Cosmic Hunt stories build on decades of research by scholars who based their work primarily on oral and written versions of folktales and legends. The current models also incorporate empirical observations of mythological motifs in prehistoric rock art. Similarities in certain rock art motifs and the reconstructed stories open a new window on the mental universe of the first humans who migrated across the Bering Strait to the New World between 30,000 and 15,000 years ago.

In the myth of Polyphemus, as its original public most likely heard it, a hunter faces one or many monsters that possess a herd of wild animals. He enters the place where the monster keeps the animals and finds his way out blocked by a large obstacle. The monster tries to kill him. The hero manages to escape by clinging to the underbelly of one of the animals.

This protomyth—revealed by three separate phylogenetic databases, many statistical methods and independent ethnological data—reflects the belief, widely held by ancient cultures, in the existence of a master of animals who keeps them in a cave and the need for an intermediary to free them. It could also be part of a Paleolithic conception of how game emerges from an underworld. At the Cave of the Trois-Frères (or "three brothers") in the French Pyrenees, frequented during the upper Paleolithic, a panel shows a small creature with the head of a bison and the body of a human, which seems to be holding a short bow. Lost in the middle of a herd of bison, another animal, similar to a bison, turns its head toward the human hybrid, and the two creatures exchange gazes. On examination, the left rear thigh of the "bison" is not the thigh of a ruminant; its proportions are much smaller, like a human thigh—so much so that archaeologist André Leroi-Gourhan took it for a human silhouette. Moreover, the artist has meticulously drawn the anus and the vulvar orifice. These two elements can be compared with some Amerindian versions of the Polyphemus story, where the man hides himself in the animal by entering its anus.

The first version of the Cosmic Hunt, the ancestor of all the other accounts of the story of Callisto, reconstructed from three different databases, would have gone like this: A man is hunting an ungulate; the hunt takes place in the sky or ends there; the animal is alive when it is transformed into a constellation; and this constellation is the one we know as Ursa Major.

This reconstruction of the Cosmic Hunt story might explain the famous Paleolithic "well scene" found in a cave in Lascaux, France. The intriguing lone black spot near the bison's withers would thus be a star. The fixedness of the animal, which does not give the impression of actually charging, would make sense if it represented a constellation rather than an action. Moreover, according to some experts, the man might be upright and the bison ascending, which echoes the rise into the sky of the protomythic animal. Finally, the black stains on the ground under the bison suggest the bloodstained autumnal leaves of the hunted animal.

Linking a mythical story and a Paleolithic image is tricky. These examples serve simply to illustrate the interpretive power of the phylogenetic method, which makes it possible to propose plausible hypotheses and to recover stories that disappeared long ago.

PRIMEVAL DRAGONS AND SERPENTS

MY CURRENT RESEARCH LENDS credibility to the out-of-Africa theory of human origins, asserting that anatomically modern humans originated in Africa and spread from there to the rest of the world. It complements phylogenetic studies by biologists that indicate the first major wave of human migration radiating from Africa followed the southern coastline of Asia, peopled Australia some 50,000 years ago and reached America from an East Asian source. Both the biological and mythological research point to a second migration reaching North America at more or less the same time from a North Eurasian source.

I recently constructed a phylogenetic supertree to trace the evolution of serpent and dragon myths that emerged during those early waves of migrations. One protonarrative that most likely predated the exodus from Africa includes the following core story elements: Mythological serpents guard water sources, releasing the liquid only under certain conditions. They can fly and form a rainbow. They are giants and have horns or antlers on their heads. They can produce rain and thunderstorms. Reptiles, immortal like others that shed their skin or bark and thus rejuvenate, are contrasted with mortal men and/or are considered responsible for originating death, perhaps by their bite. In this context, a person in a desperate situation gets to see how a snake or other small animal revives or cures itself or other animals. The person uses the same remedy and succeeds. I constructed this protomyth from five separate databases by varying both the definition of serpent/dragon and the units of analysis, including individual versions of the same tale type, types of serpents and dragons, and cultural or geographical areas.

Eventually I hope to go back even further in time and identify mythical stories that may shed light on interactions during the Paleolithic period between early *H. sapiens* and human species that went extinct. Evolutionary biologists have identified possible interbreeding with Neandertals, Denisovans and perhaps other archaic humans. Material exchanges, as well as language and mythological borrowings, may have also occurred. My more immediate goal is to expand and refine the burgeoning phylogenetic supertree of Paleolithic myths, which already includes stories of the life-giving sun as a big mammal and of women as primordial guardians of sacred knowledge sanctuaries. SA

MORE TO EXPLORE

A Cosmic Hunt in the Berber Sky: A Phylogenetic Reconstruction of Palaeolithic Mythology. Julien d'Huy in *Les Cahiers de l'AARS,* No. 16, pages 16, 93–106; 2013.

A Phylogenetic Approach of Mythology and Its Archaeological Consequences. Julien d'Huy in *Rock Art Research,* Vol. 30, No. 1, pages 115–118; May 2013.

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FROM OUR ARCHIVES

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AGRICULTURE

THE LOOMING THREAT OF FACTORY-SUPERBUGS

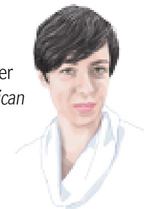
Antibiotic-resistant bacteria from livestock pose a deadly risk to people. But the farm lobby won't let scientists track the danger

By Melinda Wenner Moyer

Photographs by Patrick Cavan Brown

It wasn't until a pig nosed me in the backside, in a friendly way, that I mustered the courage to touch one. I had seen thousands of hogs over the past 18 hours, but I had been nervously keeping my hands to myself. This particular pig seemed to disapprove of my restraint. I scratched him on the crown of his pink, wiry-haired head. He snorted loudly.

Melinda Wenner Moyer is a science writer and frequent contributor to *Scientific American* and *Scientific American Mind*.



CLOSE QUARTERS: At Keith Schoettmer's Indiana farm, just weaned pigs are herded to their new home—a crowded pen.

I was in a pungent, crowded barn on a farm that raises 30,000 pigs a year in Frankfort, Ind., a sleepy farming town 45 miles northwest of Indianapolis. The farm belonged to Mike Beard, who was standing next to me. The pigs belonged not to Beard but to TDM Farms, a hog production company. Beard has a contract to raise TDM's pigs from when they are 14 days old, just weaned from their mother's milk, until the age of six months, when they are trucked to a processing plant and made into pork chops, sausages and tenderloins. The 40-by-200-foot barn housed 1,100 pigs. Because Beard is paid for the space he provides rather than by the number of pigs, "it's to the company's advantage to keep the buildings as full as they can," he explained. At 7:30 that evening, a tractor-trailer would deliver 400 more piglets, and as soon as they got settled, Beard planned to give them TDM-approved feed containing antibiotics—a necessity if they were to stay healthy in their crowded, manure-gilded home. Antibiotics also help farm animals grow faster on less food, so their use has long been a staple of industrial farming.

But there is a terrifying downside to this practice, which was one reason I had been hesitant to touch my porcine pal. Antibiotics seem to be transforming innocent farm animals into disease factories. The animals become sources of deadly microorganisms, such as the methicillin-resistant *Staphylococcus aureus* (MRSA) bacterium, which is resistant to several major classes of antibiotics and has become a real problem in hospitals. The drugs may work on farms at first, but a few microbes with the genes to resist them can survive and pass this ability to fight off the drugs to a larger group. Recent research shows that segments of DNA conferring drug resistance can jump between different species and strains of bacteria with disturbing ease, an alarming discovery. By simply driving behind chicken transport trucks, scientists collected drug-resistant microbes from the air within their cars. Early this year scientists discovered that a gene coding for resistance to a last-resort antibiotic has been circulating in the U.S. and was in bacteria infecting a woman in Pennsylvania.

Many researchers worry—and the new findings add fresh urgency to their concerns—that the abundant use of antibiotics on farms is unraveling our ability to cure bacterial infections. This latest research, scientists now say, shows resistance to drugs can spread more widely than previously thought and firms up links in the resistance chain leading from animal farm to human

IN BRIEF

Antibiotics are used more heavily in farm animals than in people. This may be the largest source of antibiotic-resistant bacteria.

Drug-resistance genes spread more widely and rapidly on farms than scientists ever thought, new discoveries show.

The agriculture industry says fears are exaggerated, whereas researchers say companies are endangering public health.

table. In 2014 pharmaceutical companies sold nearly 21 million pounds of medically important antibiotics for use in food animals, more than three times the amount sold for use in people. Stripped of the power of protective drugs, today's pedestrian health nuisances—ear infections, cuts, bronchitis—will become tomorrow's potential death sentences.

Yet the farm industry argues these worries have been wildly overblown. The idea that antibiotics "in animals directly relates to a risk to human health, we believe, has been greatly exaggerated," says Richard Carnevale, vice president of regulatory, scientific and international affairs at the Animal Health Institute, a trade group that represents veterinary pharmaceutical companies. Researchers have not directly shown that farm antibiotic use is sparking more resistant infections in people, he and other industry representatives point out. Many of the drug-resistant infections circulating in today's hospitals have never been linked to farms or animal meat.

Scientists now counter that the farm industry is the one exaggerating—even engineering—scientific uncertainty to protect their interests. "Frankly, it reminds me of the tobacco industry, the asbestos industry and the oil industry," says James Johnson, an infectious disease physician at the University of Minnesota who studies antibiotic-resistant pathogens. "We have a long history of industries subverting public health." He and other researchers admit that it is difficult to connect all the dots, but the farm industry, they say, deliberately makes it harder. Some big meat companies instruct their farmers to keep researchers away, arguing they need to keep animals free of outsiders and their diseases, which makes it impossible for scientists to solidify the science. As Tara Smith, an epidemiologist who studies emerging infections at Kent State University, tells me, the companies "want us to prove all these steps, but they're really tying our hands."

I traveled to Beard's farm, as well as two others, in an attempt to find the truth. I decided to follow in the footsteps of scientists who have been trying to trace antibiotic resistance down the long road from farm to food plate to understand whether pigs, cows, chickens or turkeys raised with antibiotics really could bring on the apocalypse—or whether these innocent-looking animals, and the billions of bacteria teeming inside them, are nothing to fear.

PROTECTED PIGS

EIGHTEEN HOURS EARLIER I had pulled into the driveway of Schoettmer Prime Pork in Tipton, Ind. The first thing that greeted me was not the sight of pigs or the pungent smell of manure. It was a menacing yellow sign: "WARNING: DISEASE PREVENTION PROGRAM. DO NOT ENTER."

Because I was there by invitation, I drove in anyway and parked two cars behind a Ford Taurus with the license plate "EATPORK." Keith Schoettmer, the farm's owner and my tour guide, waved me over from a doorway on my right.

The intimidating sign, Schoettmer explained, was among his careful efforts to prevent pathogens from sickening the 22,000 pigs he raises every year. "The old adage 'an ounce of prevention is worth a pound of cure' is never more true than on a pig farm,"

MEAT PRODUCTION: An uncastrated male pig, or boar, is pushed on a cart through a house of sows at the Schoettmer farm. His sight and smell excite the females, making them ready for artificial insemination.

said Schoettmer, whose receding white hair and broad smile reminded me of John McCain, although his accent—"manure," a frequent utterance, was "min-URR"—placed him firmly in the Midwest. Schoettmer asked me to don protective coveralls and plastic shoe covers while we walked around, too, to protect his hogs from any microbes I might be harboring.

Bacteria are everywhere, but they are more everywhere on livestock farms because everybody is literally walking around in poop. (Even though I was covered in plastic the whole time I toured Schoettmer's farm, I reeked when I checked into my hotel room hours later.) And like germs in an elementary school, the bacteria in this excrement get shared widely—they get burrowed under the fingernails of visitors who scratch the animals' heads, and they contaminate the hands of farm employees. (I never saw anyone wearing gloves.)

In 2005 researchers in the Netherlands, which has a large pig industry, determined that livestock-associated strains of MRSA were ailing Dutch pig farmers and their families. MRSA can cause deadly skin, blood and lung infections; it has circulated in hospitals for decades and, more recently, has been affecting people outside of medical settings. By 2007 one fifth of the Netherlands' human MRSA infections were identical to bacteria that had come from Dutch livestock. After this discovery, in 2008, the Dutch government announced strict policies to reduce farm antibiotic use, which then dropped by 59 percent between 2009 and 2011. Denmark, another major pork exporter, had already banned the use of antibiotics in healthy pigs in 1999; in general, Europe has taken a harder line against animal antibiotics than has the U.S.

Now scientists know that this livestock-associated MRSA is spreading throughout the U.S., too. When Tara Smith, then at the University of Iowa, heard what was going on in the Netherlands, she decided to test pigs for MRSA at a few Iowa farms where one of her colleagues, a veterinarian, had connections. "We ended up sampling 270 pigs in the first round—we just went out and swabbed a lot of pig noses and had no idea what we'd find," Smith recalls. "About 70 percent of them were positive for MRSA."

Smith and her colleagues have continued to publish a series of disturbing studies showing that MRSA is all over American hog farms. They found MRSA growing in the nostrils of 64 percent of workers at one large farm and found that feed on another farm harbored MRSA even before it got unloaded from the delivery truck. Two hundred thirty-five yards downwind of another farm, Smith found MRSA floating in the air. Other resistant bacteria have been found around poultry farms: after researchers at the Johns Hopkins Bloomberg School of Public Health drove cars, windows down, behind trucks that were transporting chickens in Maryland and Virginia, along the Delmarva Peninsula, they found antibiotic-resistant enterococci—a group of bacteria that causes 20,000 infections in the U.S. every year—in the air inside the cars, as well as resting on the top of soda cans in the cars' cup holder.

Animal poop is used to fertilize crop fields, too, which means that its bacteria are literally spread on the soil used to grow our food. A 2016 study reported that after manure from hog and dairy farms was applied to soil, the relative abundance of antibiotic-resistance genes in the dirt shot up by a factor of four. In a study conducted in Pennsylvania, people who were the most heavily exposed to crop fields treated with pig manure—for instance, because they lived near to them—had more than 30 percent increased odds of developing MRSA infections compared with people who were the least exposed. Beard runs a second business as a manure applicator—he loads 6,500 gallons of his hog manure into a single tanker truck and applies it to nearby fields—and as he noted, the process is tightly regulated. He has to perform soil tests to ensure that fields can absorb the manure nutrients, and he has to apply the manure at a slow enough rate to prevent runoff. But problems can still occur. A 2006 *Escherichia coli* outbreak in spinach was traced back to crop irrigation water that, investigators believe, had been contaminated by pig and cow manure from a nearby farm. The outbreak killed three people.

SPREADING RESISTANCE

CLEARLY, ANTIBIOTIC RESISTANCE is a problem both for people and for livestock. But how can we be sure that the two are connected and that resistance is exacerbated by on-farm antibiotic use? In 1975 the Animal Health Institute asked this very question and recruited Tufts University biologist Stuart Levy to find out. Levy and his colleagues fed low doses of the antibiotic tetracycline to a group of 150 chickens on a nearby farm that had never gotten antibiotics in their feed and monitored them to see what happened. Within a week, almost all the *E. coli* bacteria in their intestines were tetracycline-resistant. Three months in, the bacteria growing inside the chickens were also resistant to four other types of antibiotics. After four months, the bacteria growing inside chickens on the farm that *had not* been fed tetracycline also harbored resistance to the drug. When Levy and his colleagues analyzed the bacteria growing inside the farm owners, they found that 36 percent were tetracycline-resistant, compared with only 6 percent of bacteria from their neighbors. At the time, the findings came as a shock. "The idea that you would be able to give animals antibiotics at low levels and not have them develop resistance was the word of the day, and that made our study that much more interesting and unexpected," Levy recalls. (The Animal Health Institute has not funded any additional studies to confirm his findings.)

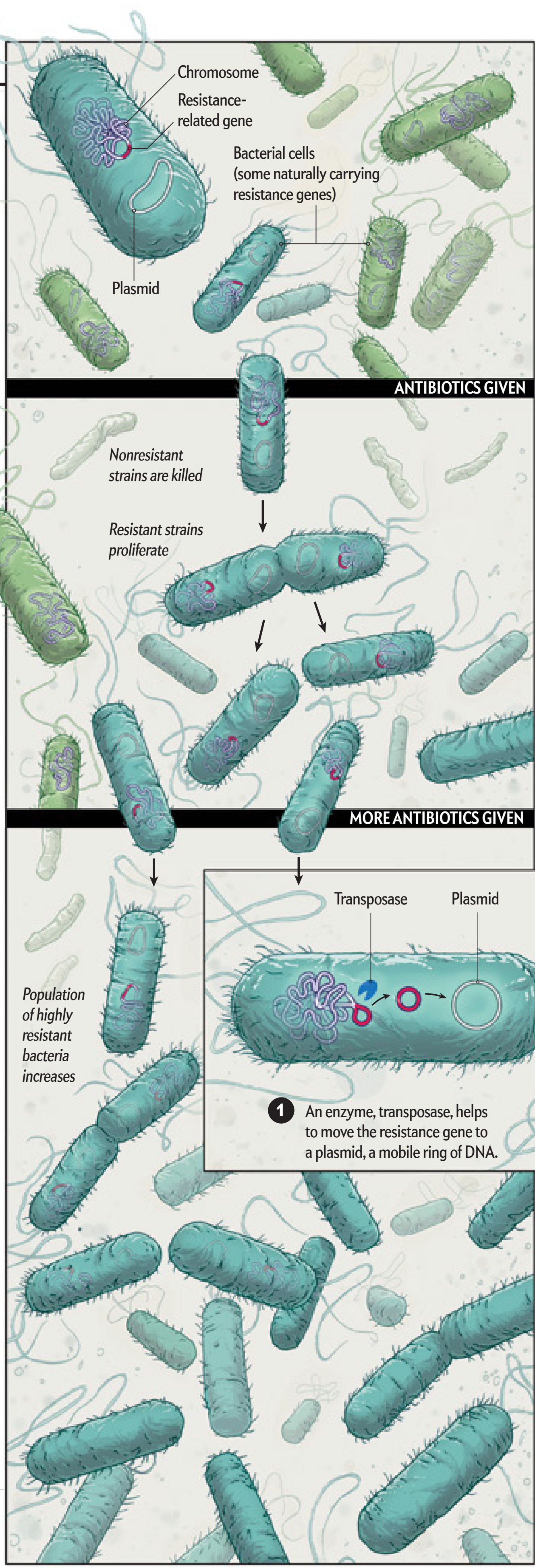
One study reported that more than 90 percent of *E. coli* in pigs raised on conventional farms are resistant to tetracycline, whereas a whopping 71 percent of *E. coli* in pigs raised on farms without antibiotics are also resistant. That is because resistance genes spread so well. In a landmark 2012 study, microbiologist Lance Price, now director of the Antibiotic Resistance Action Center at George Washington University's Milken Institute School of Public Health, and his colleagues traced the evolutionary origins of the livestock-associated MRSA that was being shared among pigs and their farmers in Europe and the U.S. by sequencing the whole genomes of 88 diverse MRSA samples. Their findings showed that this MRSA strain started out in people as a methicillin-susceptible form of *S. aureus*. Then the bacteria jumped into livestock, where they swiftly acquired resistance to methicillin and tetracycline and spread further.

At first, antibiotic resistance spreads slowly and through parent-offspring relationships—the descendants of resistant bacteria are born resistant, too. But emerging research shows that over time, resistance genes find their way onto nimble pieces of DNA that dance around the bacterial genome, and many

Illustration by Matthew Twombly

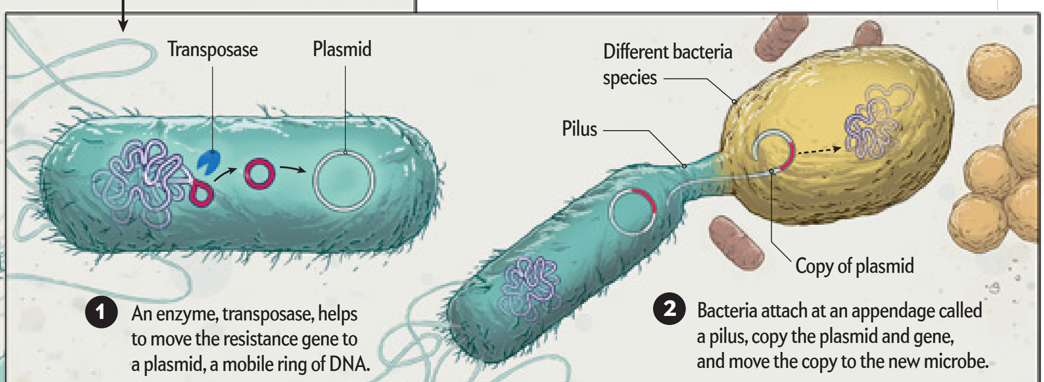
Making of a Superbug

Antibiotics were created to kill or control bacteria. In doing so, however, the drugs have become a force that shapes bacterial populations, creating conditions that favor the survival of microbes with genes that help them fight the drugs. These genes get passed to offspring in a process called vertical transfer, so a larger percentage of future generations survive. A wider danger, though, comes through a process called horizontal transfer. Resistance genes actually "jump" to different strains or species of bacteria, spreading wildly and rendering drugs ineffective when bacteria infect people.



THE VERTICAL ROUTE

Antibiotics can do a great job killing off bacteria such as *Escherichia coli* or *Staphyloccocus aureus* when the drugs are first used. But some of the microbes may, by chance, carry genes (*red*) that help them live. While susceptible bacteria die off, these hardy few survive to pass on their chromosomes, and the genes, to their offspring. Those bacteria, also able to fight the drug, pass the gene to future generations. Further doses of the antibiotic act like a filter, killing off microbes without the gene but leaving those with the gene to reproduce again and again. In this way, microbes with the gene gradually make up a greater and greater portion of the population.



THE HORIZONTAL ROUTE

Recent discoveries show how resistance genes also spread quickly from one species or strain of bacteria to another. The process starts out like the vertical method, when bacteria with resistance genes survive antibiotics. These genes can be snipped out of a chromosome by an enzyme **1** and inserted into a circle of DNA called a plasmid, which can move from one species to an entirely different one **2**.

KEEPING DANGER AWAY: On the Schoettmer farm, young pigs get a vaccine against a virus (*1*). A sign warns off visitors because they may bring infections to the animals (*2*). Pigs, aged four to five months, rest in their pens (*3*).

end up on small circles of DNA called plasmids—copies of which can easily be shared among bacteria of different species. In a 2014 study, a group of international researchers collected samples of antibiotic-resistant *E. coli* from both people and chickens. Although the bacteria were genetically different, many contained nearly identical plasmids with the same antibiotic-resistance genes. It was the organism-jumping plasmids, rather than the bacteria themselves, that spread resistance.

The fact that resistance can be spread in this way—microbiologists call it "horizontally"—changes everything. It is as if doctors suddenly discovered that Huntington's disease was not just passed down from parent to child but could also infect people who touch one another in passing. It also means that exposing one type of bacteria to one antibiotic in one place has the potential to change how other types of bacteria respond to other antibiotics in other places.

Resistance typically comes at a cost: The mutations draw down the cellular energy a microbe uses to reproduce. Individuals survive, but the whole population grows more slowly. So when bacteria stop being exposed to antibiotics, they ditch their resistance genes over multiple generations. Yet new research suggests that when bacteria are repeatedly exposed to antibiotics, they evolve resistance mutations that let them maintain higher reproductive rates—and then they stay resistant even if antibiotics are taken away. "What's really scary is that we've seen these examples in the gut where sometimes plasmids will transfer from one bacterium to another in a patient, and then they'll rearrange," says Tim Johnson, a microbiologist at the University of Minnesota College of Veterinary Medicine. "It's like it's evolving in real time in the host to become more efficient."

Multiple resistance genes also may end up on the same plasmid, so when one gene gives bacteria a survival advantage, other resistance genes come along for the ride. The extent of this co-selection, as it is called, is still a mystery; there is likely to be a lot "that we're not yet even aware of," Tim Johnson says. Yet figuring it out will be crucial for understanding how resistance spreads and how it could threaten us. Some of the antibiotics used by the farm industry are rarely or never used in humans, and the assumption—often touted by industry—is that resistance that develops to these nonhuman drugs will not pose a risk to people. But co-selection means that the use of one antibiotic could "select for resistance in another," according to Scott McEwen, an epidemiologist who studies antibiotic resistance at the University of Guelph's Ontario Veterinary College. Growing levels of resistance to a farm antibiotic may also increase levels of resistance to, say, penicillin.

Making matters worse, new research suggests that when bacteria get exposed to antibiotics, they share their resistance plasmids at a faster rate. It is as if the microbes band together in the face of a common enemy, sharing their strongest weapons with their comrades. And once bacteria become resistant, the presence of antibiotics only makes them more successful. One reason that resistant infections are so common in hospitals is because antibiotic use there is so common: the drugs kill off susceptible bacteria yet allow the resistant bugs, suddenly devoid of competition, to thrive—making it easier for them to contaminate medical equipment, staff and other patients.

GOVERNMENT COUNTERATTACK

IN THE FACE OF THESE terrifying observations, one might think the U.S. government is cracking down on agricultural antibiotic use. It is—kind of. The Food and Drug Administration released two voluntary recommendations in 2012 and 2013—the agency calls them "guidances"—that will be phased in by January 2017. In them, the agency has asked veterinary pharmaceutical companies to change the labels of their medically important antibiotics to say they should no longer be given to animals just to help them grow larger on less feed. The guidances also ask companies to stop selling feed- or water-grade antibiotics over the counter, requiring prescriptions from veterinarians instead.

Most companies have agreed to comply with the suggested rules. The problem is that a lot of livestock farms, including Schoettmer's and Beard's, say they stopped using antibiotics for growth promotion a long time ago. Their main reason for using antibiotics now, they say, is for "disease prevention and control," a purpose that will not be affected by the new rules. As long as their vets agree, farmers will still be able to mass-treat their animals with antibiotics when they fear that they may be vulnera-

3

ble to infection. "I think you'll find [this use] relatively normal in the industry," says Schoettmer, who in 2015 was crowned America's Pig Farmer of the Year by the National Pork Board. (The board was created by Congress to promote the industry and is overseen by the U.S. Department of Agriculture.) He notes that the goal is "to make sure any of these very common pathogens don't get a toehold and start to make these pigs suffer."

According to 2012 USDA data, almost 70 percent of American hog farms mass-feed antibiotics to their animals to prevent or control the spread of disease; nearly all give their pigs antibiotic-laced feed at some point in their lives. Likewise, more than 70 percent of cattle raised on large U.S. feedlots are fed medically important antibiotics, and between 20 and 52 percent of healthy chickens get antibiotics at some time as well. Yet farmers who contract with big companies may not even know when they are giving antibiotics, because they are provided with pretreated feed. When I asked Beard at what ages his pigs were given antibiotics, he said he had to contact TDM to find out.

It makes sense that animals on crowded industrial farms need antibiotics; the conditions of their lives leave them vulnerable to disease. "Density makes it more difficult to eliminate pathogens, and the risk of infection is greater," says Steve Dritz, a veterinarian at Kansas State University. The pigs I saw were crawling and lying on one another; some were snoozing in or nosing around in feces. U.S. livestock farms have been exploding in size in recent decades: in 1992 only 30 percent of farms raised more than 2,000 hogs at a time, but by 2009 farms this large accounted for 86 percent of the country's hog industry—in large part because so many small farms went out of business. There is a lot of economic pressure on these farmers. Hog prices have dropped. Companies that contract with poultry farmers insist the farms regularly upgrade their already expensive equipment and bear the cost. In 2014 only 56 percent of intermediate-sized farms reported any actual income from their farming work.

With this setup, "farmers basically have to have perfect management and perfect environments—perfect everything to keep disease out. Otherwise, they lose their flocks," Tim Johnson says. "It's not the farmer's fault, because the industry has pushed them toward this."

LINKS IN THE SAUSAGE CHAIN

THE MORNING AFTER I toured Schoettmer's farm, before leaving for Beard's, I went down to the buffet breakfast at my hotel. I paused in front of the sausage: Had any of it come from Schoettmer's pigs? He sells most of his hogs to Indiana Packers Corporation, which processes and sells the pork to local retailers. It was possible that the patties in front of me were made from some of his animals.

I took one, albeit reluctantly. What were the chances, I wondered, that this meat would give me a resistant infection? When livestock are slaughtered, their meat can get splashed with bacteria from their intestines. In a 2012 study, FDA scientists analyzed raw retail meats sold around the country and found that 84 percent of chicken breasts, 82 percent of ground turkey, 69 percent of ground beef and 44 percent of pork chops were contaminated with intestinal *E. coli*. More than half of the bacteria in the ground turkey were resistant to at least three classes of antibiotics. These microbes can cause food poisoning if meat is not cooked properly before it is eaten or if a person handling the raw meat does not wash his or her hands properly afterward.

But new research suggests that foodborne pathogens can make us sick in other ways, too. Price and his colleagues study strains of *E. coli* that he calls COPs—colonizing opportunistic pathogens. As he outlined in a 2013 paper, these bacteria most likely get inside people via food but do not, at first, cause illness; they simply colonize the gut, joining the billions of other "good" bacteria there. Later, they can infect other parts of the body, such as the urinary tract, and cause serious illness. Urinary tract infections among women at the University of California, Berkeley, between 1999 and 2000 were found to be caused by identical strains of *E. coli,* which, the authors wrote, could have arisen after the women ate contaminated food.

In recent years the CDC has successfully identified the source of contamination in large foodborne disease outbreaks only about half the time. But the origins of slow-brewing infections are far more challenging to pinpoint. Even if the sausage I ate that morning was contaminated with drug-resistant COPs, I would never know it. If I got a serious infection months later, I could never prove that it came from this breakfast. I would probably never even think about this breakfast.

This is the crux of the problem: it is difficult, if not impossible, to trace resistant infections back in time to their microbial ground zeros. "It is a long way—geographically, temporally and in other ways—from the farm to the fork," McEwen says. A hamburger can be made of meat from 100 different cows, so it is hard to pinpoint the one contributor that was contaminated. And scientists not only need to do that but also need to find out whether the way the animals were raised—whether or not they received antibiotics, for how long, at what dose and for what purpose—affected their bacteria in ways that could have spurred or worsened the outbreak. Industries also argue that farm bacteria only pose a risk to those working and living nearby, not the general public—which is why scientists try to get onto farms, to compare bacteria there with what ails the larger population.

Yet no one is gathering this kind of information. "There are very limited data collected at the farm level," concedes Bill Flynn, deputy director for science policy at the FDA's Center for Veterinary Medicine. In September 2015 the FDA, the USDA and the CDC held a meeting in which they devised a plan to start collecting more on-farm data, but they did not receive the funding they requested to actually start doing it. In fact, for fiscal year 2016, the FDA received none of the $7.1 million it requested to study antibiotic resistance in animals.

Academic scientists are desperate to go on farms and study farm animals, too, but they are rarely granted access unless they have connections. When Smith hoped to collect samples from industrial turkey farms, she contacted every single registered turkey farm in Iowa. "None of them let us on," she recalls. To study hog bacteria, Price and his colleagues have resorted to buying pig snouts at North Carolina butchers and swabbing them for bacteria because they cannot get to live animals. And remember that study in which Johns Hopkins researchers tailed chicken delivery trucks in cars? They had to conduct the study like that because they had no other way of getting close to the chickens—the researchers were not allowed on the farms.

OUTSIDE THE BOX: Seven Sons Farm in Indiana relies on extra room to keep diseases from spreading among animals and does not use antibiotics in feed.

It is not that livestock farmers are antiscience; it is that their employers, the meat companies, instruct them to keep outsiders away. A whopping 90 to 95 percent of U.S. poultry farmers and 48 percent of hog farmers (Beard being one) are contract growers—they sign contracts to raise animals for large companies like Tyson Foods, Smithfield Foods or Perdue Farms. Farmers are beholden to these companies because they undertake a huge amount of debt to start their business—a new poultry or hog farm costs a farmer about $1 million—yet they do not earn any money without a company contract; often farmers have only one choice of employer because a single company operates in their area.

Yet these company contracts—Scientific American obtained a recent contract from a former grower for Pilgrim's Pride, the largest chicken producer in the U.S.—contain clauses about animal protection, instructing farmers to "limit the movement of non-essential people, vehicles and equipment" around the farms. My visit to Beard's and Schoettmer's farms was preapproved by the National Pork Board. But when West Virginia poultry grower Mike Weaver invited a journalist onto his farm several years ago and his employer found out, "I was forced to attend 'biosecurity retraining' and was delayed receiving a new flock an extra two weeks, which amounts to a loss of revenue of around $5,000 for me," he says. Price, as a scientist, convinced a handful of farmers to grant him farm access years ago, but then, he recalls, they "lost their contracts."

Despite repeated requests, the American Farm Bureau Federation, the farm industry trade group, and Smithfield Foods, the world's largest hog producer and pork processor, declined to comment for this article and address the issue of whether industries were keeping scientists off farms.

Whatever the reason, the lack of data has made it easier for industry to fight regulations. In 1977, soon after Levy's study was published, the FDA announced that it was considering banning several antibiotics from animal feed over safety concerns. In the 39 years since, the industry has fought hard against these plans by arguing there was no definitive proof of harm. These arguments ultimately caused the FDA to change tactics, Flynn says, and to pursue the voluntary guidances instead.

But the disease-control exemption is a gaping hole in the guidances, many complain. "Do I think the total volume of antibiotic use will go down? I absolutely do not," says H. Morgan Scott, a veterinary epidemiologist at Texas A & M University. In fact, antibiotic sales to farms have increased each year since the draft guidances were announced. In 2014 the nonprofit Pew Charitable Trusts analyzed the drug labels of all 287 antibiotic products that will be affected by the guidances and found that farmers will still be able to administer one quarter of the drugs at the same dosages and with no limits on treatment duration—as long as they say they are using them to prevent or control disease. Even the Animal Health Institute's Carnevale says the FDA guidances "could change the overall picture of how [antibiotics] are used, but whether [they're] going to affect total quantities of antibiotics remains to be seen."

The requirement for veterinary prescriptions may not put a dent in antibiotic use, either. Many veterinarians prescribe and sell antibiotics for a profit or work closely with the food or pharmaceutical industries. A 2014 Reuters news investigation reported that half of all the veterinarians who advised the FDA on antibiotic use in food animals in recent years had received money from drug companies. "There are a lot of veterinarians who are attached to industry, who have a conflict of interest and who are beholden to the large producers—so they are inclined to go along with the status quo," James Johnson says.

Several members of the U.S. Congress, including New York

SCIENTIFIC AMERICAN ONLINE A scientist explains why factory farms overuse antibiotics at ScientificAmerican.com/dec2016/drugs-bugs

State Representative and microbiologist Louise Slaughter, have introduced bills to more tightly regulate antibiotic use on farms. Slaughter has pushed for her Preservation of Antibiotics for Medical Treatment Act for more than a decade. It has been supported by 454 organizations, including the American Medical Association. But after being referred to the Health subcommittee of the House Energy and Commerce Committee, the bill never reaches a vote.

One committee member who does not support the bill at this point, Representative Tim Murphy of Pennsylvania, has gone on record warning against the continued low-level use of antibiotics in food animals and the dangers that resistant bacteria pose to our food supply, says his press secretary, Carly Atchison. But he does not think the bill "strikes the appropriate balance needed in the use of medically important antibiotics in agriculture and farming," Atchison says. There is also significant opposition to the bill from industry. The National Chicken Council spent $640,000 in 2015 to lobby, in part, against antibiotic-related legislation, and the Animal Health Institute spent $130,000, according to records from the nonprofit Center for Responsive Politics. Center data also show that veterinary pharmaceutical companies or livestock farming organizations have made campaign donations of more than $15,000 to more than half of the members of the Health subcommittee. "The trade organizations have been down there saying, 'You can't show it's us—that we're causing the resistance,'" says Patty Lovera, assistant director of the nonprofit Washington, D.C.–based Food and Water Watch. "That has really gummed up the works for a long time."

A SMALL SOLUTION

AFTER I LEFT Beard's farm, I drove two hours to my final destination: Seven Sons Farms in Roanoke, Ind., which raises pigs on pastures and woodlands without antibiotics. A decade ago Seven Sons was a lot like the two farms I had just seen—it raised 2,300 hogs a year for Tyson Foods, regularly using drugs. But the family was worried about health effects, so it made some changes. In 2000 Seven Sons became what it calls a regenerative diversified farm, and today it raises about 400 pigs, 2,500 egg-laying hens and 120 forage-fed cattle on 550 acres of pasture.

Blaine Hitzfield, the second of the farm's seven namesake sons, took me on a short tour. I saw fewer than a dozen hogs lounging around a half-acre expanse of dirt and grass. Hitzfield did not ask me to wear coveralls, and he was not concerned that I had come directly from another hog farm. The animals on his farm, he explained, are hardier than those raised in confinement: not only do they have more space and mobility, but they are also weaned later so that they develop stronger immune systems. Nature helps as well. "The sun is a wonderful sanitizer, and the mud does wonders for keeping the parasites off," he said. (If a pig does get sick, Seven Sons treats it with antibiotics but then sells it at auction rather than with their label.) His claims have research behind them. In a 2007 study, Texas Tech University researchers reported that pigs that had been raised outside had enhanced activity of bacteria-fighting immune cells called neutrophils when compared with animals raised inside.

Hitzfield conceded that Seven Sons' approach could be hard to envision as the future of industrial farming. "Conventional-minded farmers would say, 'This is ridiculous; it would never work; it's not scalable'—and to a certain extent they're right," he said. Seven Sons is just a small prototype, but Hitzfield said that with time and more research, much bigger versions would be possible. "On a per-acre basis, we're much more productive than we've ever been," he added.

Some industrial farms are making changes, thanks in large part to consumer demand. They are not becoming small, diversified operations. But in February 2016 Perdue Farms announced that two thirds of its chickens would be raised without medically important antibiotics; Tyson Foods has pledged to stop using human antibiotics to raise its U.S. chickens by September 2017. Broiler chickens are far easier to industrially raise without antibiotics than pigs, cows or turkeys because they are slaughtered at younger ages.

But demand is driving some large-scale pork producers to scale back, too. "It is not an easy thing to do," says Bart Vittori, vice president and general manager for pork at Perdue Farms' food division, which has an arm called Coleman Natural Foods. Coleman raises pigs on a vegetarian, antibiotic-free diet. "The demand is out there. Our consumers are smarter than ever, more informed than ever, asking more questions than ever," Vittori says. The meat that comes out of Niman Ranch, a network of more than 725 family-run hog, lamb, cow and egg-laying hen farms throughout the U.S., has also been raised without drugs.

Products from Coleman, as well those from niche farms such as Seven Sons and Niman Ranch, are out of the financial reach of many Americans today. But the more that consumers demand antibiotic-free meat, the more supply there will be and—if basic economics holds true—the less it will cost.

Scientists still have many, many questions about antibiotic resistance—questions that may never get answered if food companies continue to ban outsiders from their farms. Even so, the weight of the evidence points strongly toward reducing antibiotic use on farms, relying instead on novel infection-control regimens or age-old strategies such as providing animals with ample space. Until some of those changes occur, researchers and the rest of us will continue to worry about the growing strength of foodborne bacteria and the increasing weakness of our medicine against them. SA

MORE TO EXPLORE

Methicillin-Resistant *Staphylococcus aureus* in Pigs and Farm Workers on Conventional and Antibiotic-Free Swine Farms in the USA. Tara C. Smith et al. in *PLOS ONE,* Vol. 8, No. 5, Article No. e63704; May 7, 2013.

Prevalence of Antibiotic-Resistant *E. coli* in Retail Chicken: Comparing Conventional, Organic, Kosher, and Raised without Antibiotics. Version 2. Jack M. Millman et al. in *F1000Research,* Vol. 2, Article No. 155. Published online September 2, 2013.

Multidrug-Resistant and Methicillin-Resistant *Staphylococcus aureus* (MRSA) in Hog Slaughter and Processing Plant Workers and Their Community in North Carolina (USA). Ricardo Castillo Neyra et al. in *Environmental Health Perspectives,* Vol. 122, No. 5, pages 471–477; May 2014.

Livestock-Associated *Staphylococcus aureus:* The United States Experience. Tara C. Smith in *PLOS Pathogens,* Vol. 11, No. 2, Article No. e1004564; February 5, 2015.

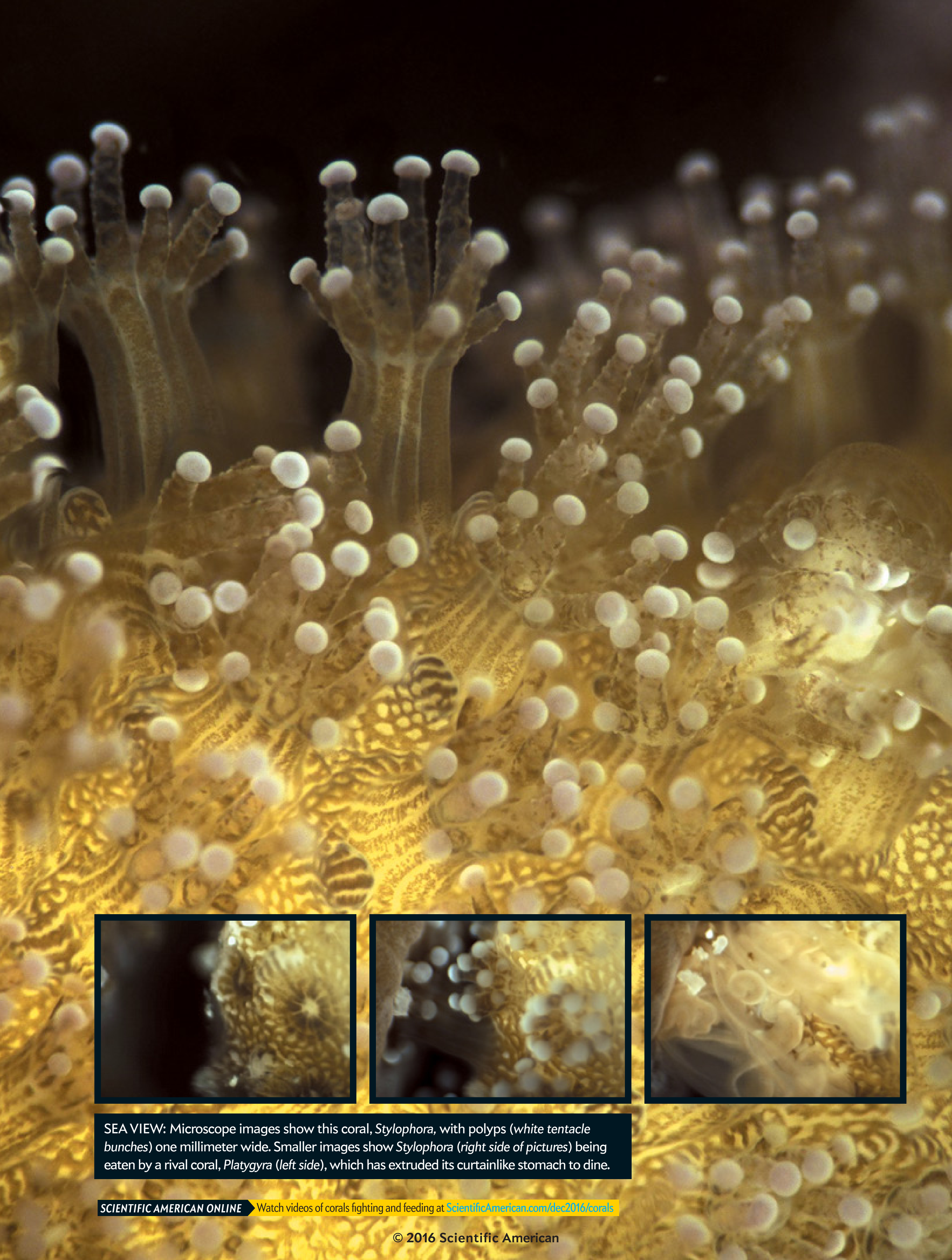
Detection of Airborne Methicillin-Resistant *Staphylococcus aureus* Inside and Downwind of a Swine Building, and in Animal Feed: Potential Occupational, Animal Health, and Environmental Implications. Dwight D. Ferguson et al. in *Journal of Agromedicine,* Vol. 21, No. 2, pages 149–153; 2016.

FROM OUR ARCHIVES

The Enemy Within. Maryn McKenna; April 2011.

Pills for Pigs: Just Say No. Keeve Nachman; Forum, March 2016.

scientificamerican.com/magazine/sa



SEA VIEW: Microscope images show this coral, *Stylophora,* with polyps (*white tentacle bunches*) one millimeter wide. Smaller images show *Stylophora* (*right side of pictures*) being eaten by a rival coral, *Platygyra* (*left side*), which has extruded its curtainlike stomach to dine.

SCIENTIFIC AMERICAN ONLINE Watch videos of corals fighting and feeding at ScientificAmerican.com/dec2016/corals

EYES IN THE DEEP

A new seafloor microscope is revealing life-and-death battles between hair-thin creatures *By Josh Fischman*

Underneath the waves of the Pacific Ocean, scientists in 2015 watched a slow and surprising dance of death in unprecedented detail.

Andrew D. Mullen, a graduate student who works with oceanographer Jules Jaffe at the University of California, San Diego's Scripps Institution of Oceanography, was peering at a dying coral reef near the island of Maui in Hawaii. The reef had just been "bleached"—symbiotic algae that live in each tiny coral polyp got too hot, and the coral had expelled them. "The polyps turned white, and they were weak. But they were still alive," Mullen recalls.

Then doom arrived, in the form of green threads of other, invasive algae that drifted onto ridges of calcium compounds between the polyps. "Even weak coral polyps should be able to resist algae," Mullen says. But researchers had never seen how, in the wild, algae settle the in-between spaces and over months expand to cover the polyps. "Once they are overgrown, corals don't stand a chance," he explains. "They are covered in a green film, and at that point, they're dead."

This life-and-death waltz occurs on a minuscule stage. Each polyp is about one millimeter wide. The invading algae filaments can be a twentieth of a millimeter—similar to the width of a human hair—and the symbiotic algae expelled by the corals were 10 times smaller. Mullen and Jaffe were able to see all of them using a new kind of magnifier in a waterproof housing: the Benthic Underwater Microscope, the first instrument powerful enough to get real-time views of these creatures at the bottom of the sea.

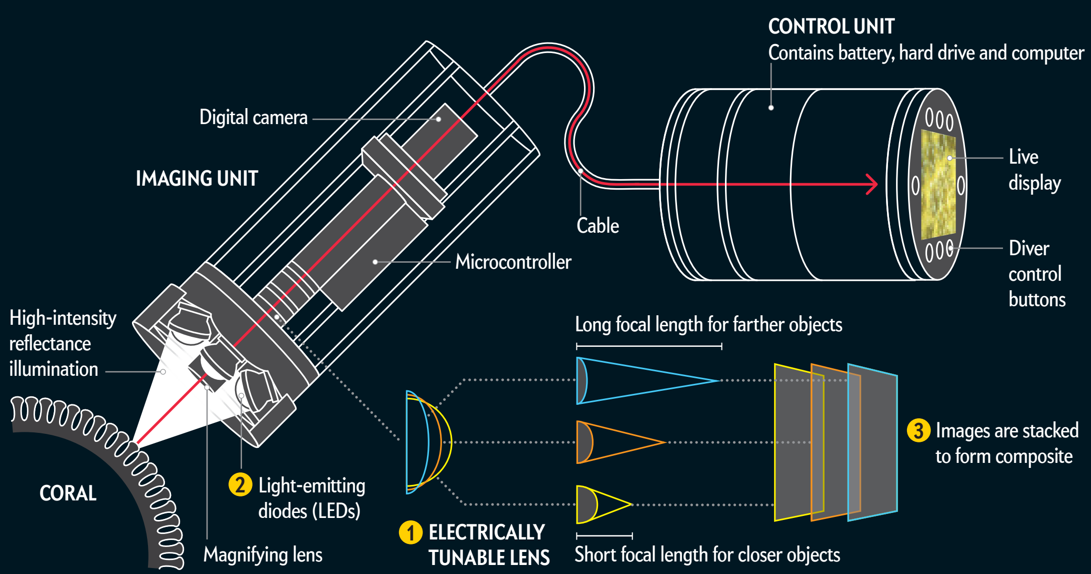
Jaffe and other ocean scientists had been able to see coral polyps close up before but only in the laboratory. On the seafloor, conditions are too dark and difficult for ordinary microscopes to produce clear images. Mullen's solution was to mount several bright LED lights around the device and to use an electrically adjustable focusing lens with a flexible polymer that rapidly flattens or thickens to keep a tiny object in sharp view, like the lens of a real eye.

The lens has shown not just death but also strategies for life. Jaffe and Mullen have watched battles between competing corals in which one digests its neighbor (*opposite page*). This does not occur, however, when the corals are of the same species, indicating the animals somehow sense their kin. How this happens remains to be seen, but with newly opened eyes, the scientists are certainly going to look. SA

Josh Fischman is a senior editor at *Scientific American.*

Underwater Microscopy

The seafloor is anathema to microscopy. Down there, dark waters and shifting currents conspire to make any minuscule object a blurry smear of motion with most lenses. The Benthic Underwater Microscope's unique design solves these problems. Its centerpiece is a deformable lens (1) that can change its shape every few milliseconds, flattening or bulging to adjust focal length and keep images sharp. To illuminate targets, the system uses submillisecond light pulses from a ring of LEDs (2), providing rapid, minimally disruptive exposures free of motion blur. By combining exposures taken at different focal lengths, a single image can be made in which all parts of a subject are in focus (3).



COURTESY OF JAFFE LABORATORY FOR UNDERWATER IMAGING *Scripps Institution of Oceanography, University of California, San Diego (photographs)*; SOURCE: "UNDERWATER MICROSCOPY FOR IN SITU STUDIES OF BENTHIC ECOSYSTEMS," BY ANDREW D. MULLEN ET AL., IN *NATURE COMMUNICATIONS*, VOL. 7, ARTICLE NO. 12093. PUBLISHED ONLINE JULY 12, 2016 *(illustration)*

Illustration by John Grimwade

RECOMMENDED

By Clara Moskowitz

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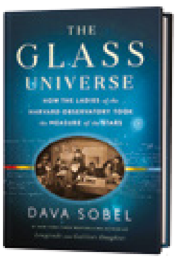
The Glass Universe:

How the Ladies of the Harvard Observatory Took the Measure of the Stars

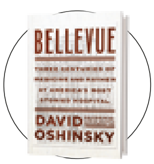
by Dava Sobel. Viking, 2016 ($30)



Originally hired as human "calculators" to offer mathematical assistance to the scientists at the Harvard College Observatory starting in the late 1800s, a group of intrepid women soon began interpreting the data they were meant to crunch. They painstakingly analyzed the photographic plates of the heavens collected night after night at the observatory's telescopes. They were able to use their analyses to classify stars based on the characteristics of their light, discover patterns among stars whose brightness varies periodically and identify double-star systems, among other achievements. Through letters, journal entries and historical documents, science writer Sobel sketches an inspiring portrait of these women who helped to pave the way for female astronomers at a time when women were not even allowed to vote, let alone participate in most academic fields. She brings to life characters such as Henrietta Swan Leavitt, Annie Jump Cannon and Antonia Maury, whose contributions were so noteworthy they gained some recognition from the wider field, as well as Edward Charles Pickering, the observatory director who recruited more than 80 women and championed their successes.

Bellevue: Three Centuries of Medicine and Mayhem at America's Most Storied Hospital

by David Oshinsky. Doubleday, 2016 ($30)



"Under-budgeted, understaffed, and crammed with patients" have been constants throughout the nearly 300-year history of New York City's Bellevue Hospital, the oldest continuously operating hospital in the U.S. Historian Oshinsky tells the story of this home to the city's ailing immigrants and poor and its intersection with the histories of American health care and New York City. Bellevue has weathered many trials over the years, including public health crises from yellow fever, typhus, Spanish flu and AIDS—epidemics made worse at the hospital by classism, racism and xenophobia, which drove wealthier New Yorkers and their money away from struggling Bellevue. But the hospital's story is also one of innovation and progress: it opened the U.S.'s first nursing school in 1873 and developed the nation's first modern pathological laboratory course in 1878.

—Ryan F. Mandelbaum

Citizen Scientist: Searching for Heroes and Hope in an Age of Extinction

by Mary Ellen Hannibal. The Experiment, 2016 ($25.95)

"Citizen science is taking off as never before, and it is needed as never before," writes journalist Hannibal in this celebration of nonexperts' contributions to science. By monitoring whales offshore, hawks in the sky, sea stars in tide pools and galaxies in the universe, science-interested volunteers are contributing to global studies that desperately need their additional manpower and brainpower. And technology these days, particularly in the form of smartphones, is allowing more people to collect more useful data than ever before. The result is that folks who used to be part of the landscape of subjects studied by science are becoming "co-creators" of science, which benefits them and the research they contribute to, Hannibal writes. An avid citizen scientist herself, she traces the roots of amateur research and explores its effects both on the world at large and in her own life, especially in helping her deal with the recent unexpected death of her father.

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

Born This Way

A new battle over sexual orientation

By Michael Shermer

When did you choose to become straight?

Say what?

By demographic distribution (about 95 percent of the population identifies as heterosexual), the majority of you reading this column are straight. You no more chose this sexual orientation than gays or lesbians choose theirs. Yet a new study published in the fall issue of the nonpeer-reviewed journal *The New Atlantis* by Johns Hopkins University's Lawrence S. Mayer and Paul R. McHugh on "Sexuality and Gender" claims that "our scientific knowledge in this area remains unsettled," that there is no "scientific evidence for the view that sexual orientation is a fixed and innate biological property," and that no one is "born that way." This sounds so 1990s, the last time the gender wars heated up. What's going on here?

One clue comes from the journal's co-publisher, the Ethics and Public Policy Center (EPPC), "dedicated to applying the Judeo-Christian moral tradition to critical issues of public policy." Already we're off the science page. EPPC scholars, its Web page continues, "have consistently sought to defend and promote our nation's founding principles—respect for the inherent dignity of the human person, individual freedom and responsibility, justice, the rule of law, and limited government."

Shouldn't such principles apply to everyone regardless of whether or not their sexual orientation is biologically determined? Of course, and in most Western countries today they do. But in Judeo-Christian America, the argument goes like this: The Bible says that homosexuality is a sin (Leviticus 20:13). If sexual orientation has a strong biological component, then gays and lesbians can hardly be held morally culpable for their sinful ways. But if it's a choice, then they can be rehabilitated (through "conversion therapy") and forgiven ("love the sinner, hate the sin" goes the popular trope). Evangelist Jimmy Swaggart articulated the logic this way: "While it is true that the seed of original sin carries with it every type of deviation, aberration, perversion, and wrongdoing, the homosexual cannot claim to have been born that way any more than the drunkard, gambler, killer, etc."

While the authors of the *New Atlantis* article are not this crude and overtly bigoted in their conclusions, according to geneticist Dean Hamer, emeritus at the National Institutes of Health, "it is a selective and outdated collection of references and arguments aimed at confusing rather than clarifying our understanding of sexual orientation and gender identity." For example, Mayer and McHugh claim that the concept of sexual orientation is "ambiguous" and that there are "no agreed-upon definitions for purposes of empirical research." Not so. The American Psychological Association defines sexual orientation as "an enduring pattern of emotional, romantic and/or sexual attractions to men, women or both sexes," and as Hamer points out, sexual orientation is far less "ambiguous" than personality traits like "self-esteem" and "warmth" that scientists study without religious and political ramifications.

Mayer and McHugh also appear to be data snooping when they reference only one of six studies in the peer-reviewed literature of the past 16 years that employ proper probability-sampling methods, "and it just so happens to be the one with the lowest estimate of genetic influence of the entire set," Hamer says. Moreover, the entire article is gainsaid by a massive meta-analysis study by Northwestern University psychologist Michael Bailey and his colleagues published in the September issue of the peer-reviewed journal *Psychological Science in the Public Interest,* showing that "there is considerably more evidence supporting nonsocial causes of sexual orientation than social causes." Evidence includes: "moderate genetic influences demonstrated in well-sampled twin studies; the cross-culturally robust fraternal-birth-order effect on male sexual orientation; and the finding that when infant boys are surgically and socially 'changed' into girls, their eventual sexual orientation is unchanged (i.e., they remain sexually attracted to females). In contrast, evidence for the most commonly hypothesized social causes of homosexuality—sexual recruitment by homosexual adults, patterns of disordered parenting, or the influence of homosexual parents—is generally weak in magnitude and distorted by numerous confounding factors."

The problem with any area of research that intersects with religion or politics is the possibility of motivated reasoning and the confirmation bias, or as the Bible says (Matthew 7:7): "Seek and ye shall find." Where concepts determine percepts, ideology trumps facts and science suffers. SA

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Illustration by Izhar Cohen

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

Citrus Be the Place

Regarding Florida, orange you glad I didn't say Lantana?

By Steve Mirsky

Home of Hurricanes. The Invasive Species State. Land of the Rising Sea. Live Free or Die in a Sinkhole. Any of these phrases could proudly serve as the officially legislated nickname for Florida. But the legislature in Tallahassee seems really married to the Sunshine State. Even though Arizona, California, Nevada, New Mexico and Texas all get more sunshine than Florida does, a knowledge nugget I unearthed in the new book *Oh, Florida!: How America's Weirdest State Influences the Rest of the Country* (St. Martin's Press).

The book's author, *Tampa Bay Times* journalist Craig Pittman (an apt name for someone revealing the reality of a place famous for orange juice), is a Florida native. Which, as he points out on page 2, puts him in the minority: "Only about a third of Florida's 19 million residents are natives. Some of those six million—nobody knows how many—are kids born in the last decade." The true number will stay under wraps until the 2020 census, the findings of which I just realized will spawn innumerable "Hindsight is 2020" leaden jokes from news anchors.

The population boom in the Shady Land Deal State is one reason I'm so leery of hitting the highway when I visit. It seems like driving every other car is a youngster distracted by the competing demands of texting and applying acne unguents. While every other-other car is piloted by a member of the Greatest Generation, whose reflexes and eyesight have been on the decline since Ike handed over the keys to the White House. Pittman notes that as of 2012, Florida had 65,000 licensed drivers between 91 and 100, and the state "had 455 licensed drivers who were one hundred or older." Yikes.

Speaking of the White House and bad driving, by the time you read these words Florida may have once again T-boned the nation. (See presidential elections of 1876 and 2000.) I can't know for sure, because I'm writing in early October, and I don't have a crystal ball. But I could buy one in the Florida town of Cassadaga, which, Pittman writes, "has so many crystal balls per capita that it's known as the Psychic Capital of the World." Fortunately, Florida is also home to James Randi, the former magician and escape artist who has devoted his life's second act to making such claims of paranormal phenomena disappear.

Oh, Florida! covers the state's chicanery (including political and business corruption, often intertwined) and general goofiness (including the history of Disney's outsize influence). But Pittman squeezes in a lot of science, too—for example, invasive species. "Scientists say Florida has more invasives than any other state," Pittman writes.

Iguanas are a growing nuisance—I've seen half a dozen cavorting in a patch of sandy soil at the incredibly busy corner of Glades Road and U.S. 441, for you West Boca Raton fans. But the most famous invasive now has to be the Burmese python, which is all over the Everglades and, Pittman says, wiped out "the rabbits, raccoons, and foxes that lived there. Pythons have tried to gobble up the alligators too, but the gators fight back."

You may have seen the 2005 photograph that went viral of a python-alligator mash-up. The 13-foot snake swallowed the six-foot crocodilian, which spent its, and its host's, last moments clawing its way out, "making the snake explode," Pittman describes. See the book for stories about the invasive hogs, monkeys and GALS—giant African land snails—smuggled in for their alleged healthful mucus, which people drank and got sick from.

The sea around Florida has risen about eight inches "since reliable record keeping began in 1880," Pittman offers. And the rise is accelerating. Meanwhile the land "is about as solid as Swiss cheese. Geologists call it karst—limestone caverns that easily crumble." Which means sinkholes. One in Winter Park in 1981 swallowed "250,000 cubic yards of soil, five Porsches from a foreign car repair shop, the deep end of an Olympic-size swimming pool, chunks of two streets and a three-bedroom home."

I'll be heading down to Florida for Thanksgiving. I want to see it while it's still there. SA

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Illustration by Matt Collins

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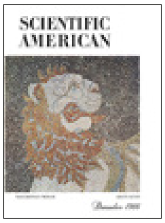
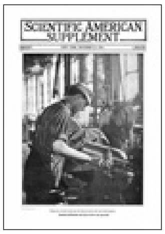


1966



1916

1866

1966 Noise

"The noises of our daily life have been blamed variously for the high divorce rate, social conflict, indigestion and other organic disabilities, nervous breakdown, high blood pressure, heart failure and even insanity. Most of these allegations arise from overvivid imaginations. Studies of the annoyance effect have been conducted among people living in noisy areas: in central London, near the London airport and in several U.S. cities, some of them near military air bases. About a fourth of the inhabitants apparently are able to live happily next to elevated railroads, trucking routes, airplane flight paths and other loud noise sources. At the other extreme, about a tenth of those interviewed seem to be disturbed by almost any noise not of their own making."

1916 Thomas Alva Edison: An Interview on Labor

"'Americans have a way of blundering into high efficiency. Take, for instance, our low-priced automobiles—they are something that Europe cannot understand. We pay more for labor, but an American laborer is worth more than a foreign laborer. Psychologists would do well to study the mental equations of different countries. When I went through Europe I took the personal equations of the men. In France they were quicker to pay attention to my automobile horn than in any other country. In Switzerland you could nearly run a man down before he heard the horn. It represents the peculiar mental state of the people.'"

Hog Cholera

"'Hog' is a term of derision or contempt, by the man in the city. But the farmer calls his hogs 'mortgage-lifters,' because the revenue derived from swine raising is responsible for much of farming prosperity. At the present time there are 68,047,000 hogs in the United States. Their value is $571,890,000. The average loss annually, due to hog cholera, during the last forty years is estimated at not less than $40,000,000. A series of experiments looking to the eventual control of hog cholera by quarantine, sanitary measures, and preventive serum treatment, extended during 1914, 1915 and 1916, has demonstrated the possibility of saving from 85 to 90 per cent of the animals."

Urban Snow Removal

"The problems of snow fighting in New York City are considered long in advance by the Department of Street Cleaning, just as the General Staff of an army develops its strategy and plans campaigns long before war is declared. Where motor trucks with plows are not employed, the gangs of emergency men with scrapers do similar work, shoving masses of snow [*see illustration*]. Motor-driven snow plows are attached to the front of five-ton trucks. The large fleet of tractors employed for garbage removal is suitable for this task."

For a look at urban engineering in 1916, see the slide show at www.ScientificAmerican.com/dec2016/urban-engineering


1916: Emergency snow removal. A crew with an old horse-drawn cart works alongside the latest model of snowplow.

SCIENTIFIC AMERICAN, VOL. CXV, NO. 25; DECEMBER 16, 1916

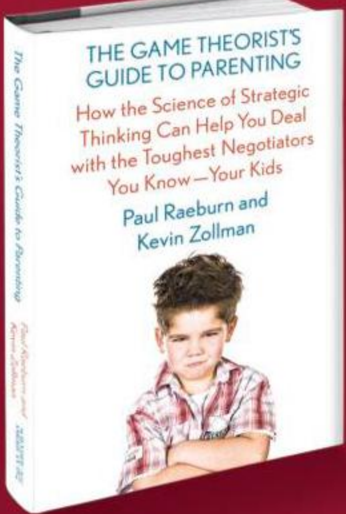
1866 Ice Skates for Fun

"That skating has become a fashionable exercise, is evident from the following statements as to the materials consumed during the present year, in one skate factory at Worcester, Mass.: two tons of brass, 5,000 gross of screws; 50,000 brass thimbles, 1,000 pounds of German silver, nearly six tons of rosewood, and ten tons of steel, worked up by 35 men and women into 25,000 pair of skates."

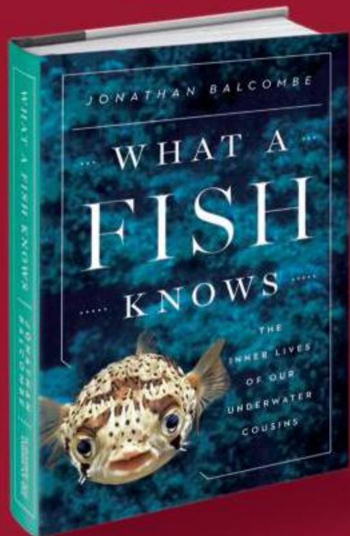
Coat of Many Colors

"'Never select colors in the evening,' is an old maxim, whose value can be attested by many a disappointed purchaser, who, ignorant or disregarding this advice, and deeming himself the favored possessor of some tint of rare excellence, discovers on the return of daylight a color far from equalling his anticipations. The cause of this inconstancy is explained in a late article in the *Photographic News*. From the spectral analysis, we learn that the flames of our lamps or gas lights contain sodium, which, in burning, yields a yellow flame, as strontium gives a red, and iridium a blue flame. This flame alters the nature of colors, deepening the hues of some and extinguishing others."

THIS HOLIDAY SEASON GIVE THE BEST IN SCIENCE

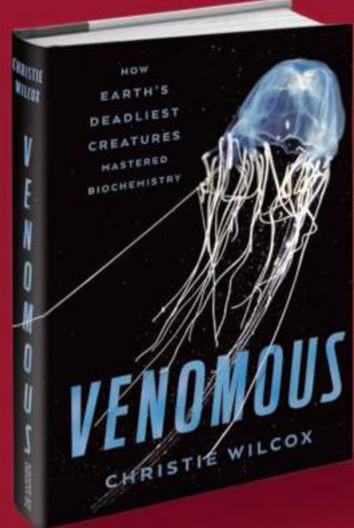


"Unlike most parenting books, . . . this one is based on actual research into how humans behave."
—Laura Vanderkam, *The Wall Street Journal*

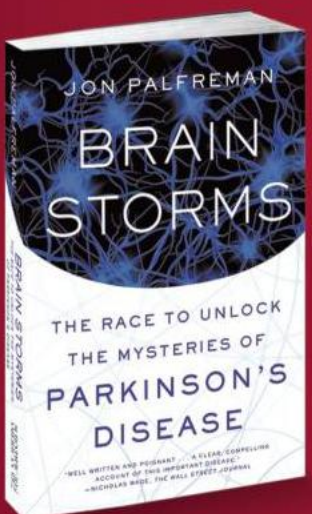


A *New York Times* Bestseller

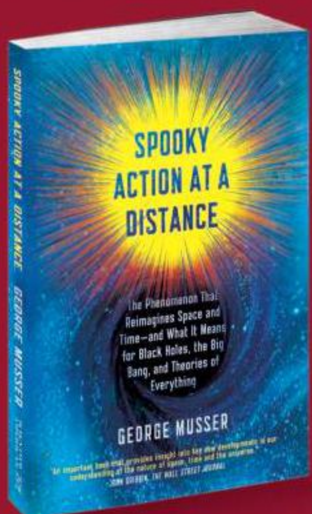
"Balcombe makes a persuasive case that what fish know is quite a lot."
—Elizabeth Kolbert, *The New York Review of Books*



"A vibrant tour through [an] exciting field."
—Jennie Erin Smith, *The Wall Street Journal*

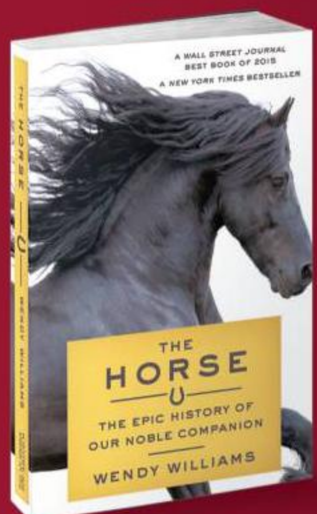


"Well worth checking out, whether you are a new or old patient, a significant other of someone with Parkinson's disease, or simply a curious reader."
—Anna Tan, *Parkinson's News Today*



Long-listed for the 2016 PEN/E. O. Wilson Literary Science Writing Award

"A highly enjoyable tour-de-force."
—David Eicher, *Astronomy*



A *Wall Street Journal* Best Book of 2015
A *New York Times* Bestseller
A *New York Times Book Review* Editors' Choice

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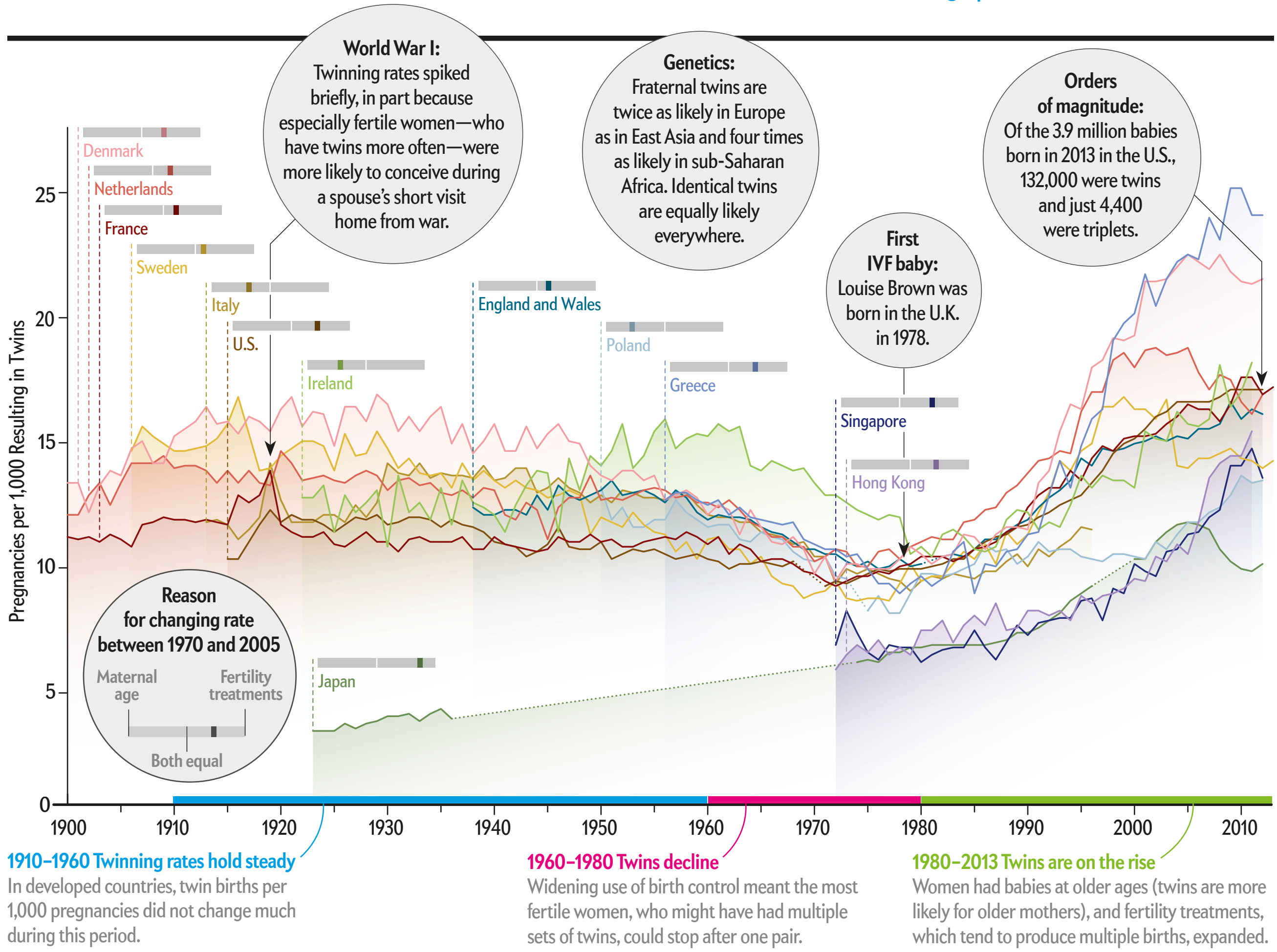
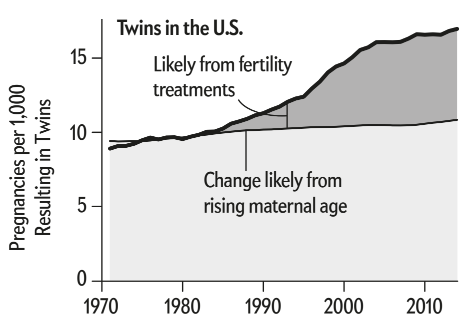


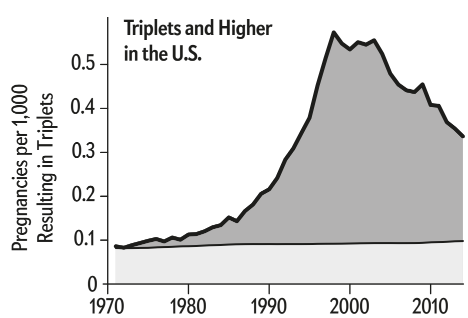
Is the Rise in Twin Births Cresting?

Fertility procedures have pushed multiple births higher, prompting policy changes

Since the 1970s more and more twins have been popping up across the developed world (*large graph*). Women have been having babies at older ages, so more are becoming pregnant at the natural peak age for twins: about 35. And fertility treatments have become more common, which boosts the chances of twins further (*bars above graph*). Because multiple births are dangerous for both mothers and babies, public health officials would like to reverse the trend. Sweden, Denmark and a few other countries are turning their twinning rates around with guidelines or regulations that restrict the number of embryos implanted during most in vitro fertilization (IVF) procedures (*small graphs*). That change has also cut the rate of triplets significantly. —*Katie Peek*

Fertility Treatments or Aging Mothers?
In the U.S., multiple births rise slightly as maternal age goes up (*thin line*), but fertility treatments push the rates much higher (*heavy line*). Since about 2000, however, the elevated triplets rate has dropped, in large part because fewer doctors are implanting three or more embryos during IVF procedures. Implanting only one embryo could lower the twinning rate, too.





SOURCES: "TWINNING RATES IN DEVELOPED COUNTRIES: TRENDS AND EXPLANATIONS," BY GILLES PISON ET AL., IN *POPULATION AND DEVELOPMENT REVIEW*, VOL. 41, NO. 4; DECEMBER 2015 (*large graph*); "FERTILITY TREATMENTS AND MULTIPLE BIRTHS IN THE UNITED STATES," BY ANIKET D. KULKARNI ET AL., IN *NEW ENGLAND JOURNAL OF MEDICINE*, VOL. 369, NO. 23; DECEMBER 5, 2013 (*structure of small graphs*); NATIONAL CENTER FOR HEALTH STATISTICS, 1971–2014 (*data in small graphs*)

Graphic by Katie Peek