5 SCIENTIFIC FACTS (THAT PEOPLE OFTEN GET WRONG)

SCIENTIFIC AMERICAN

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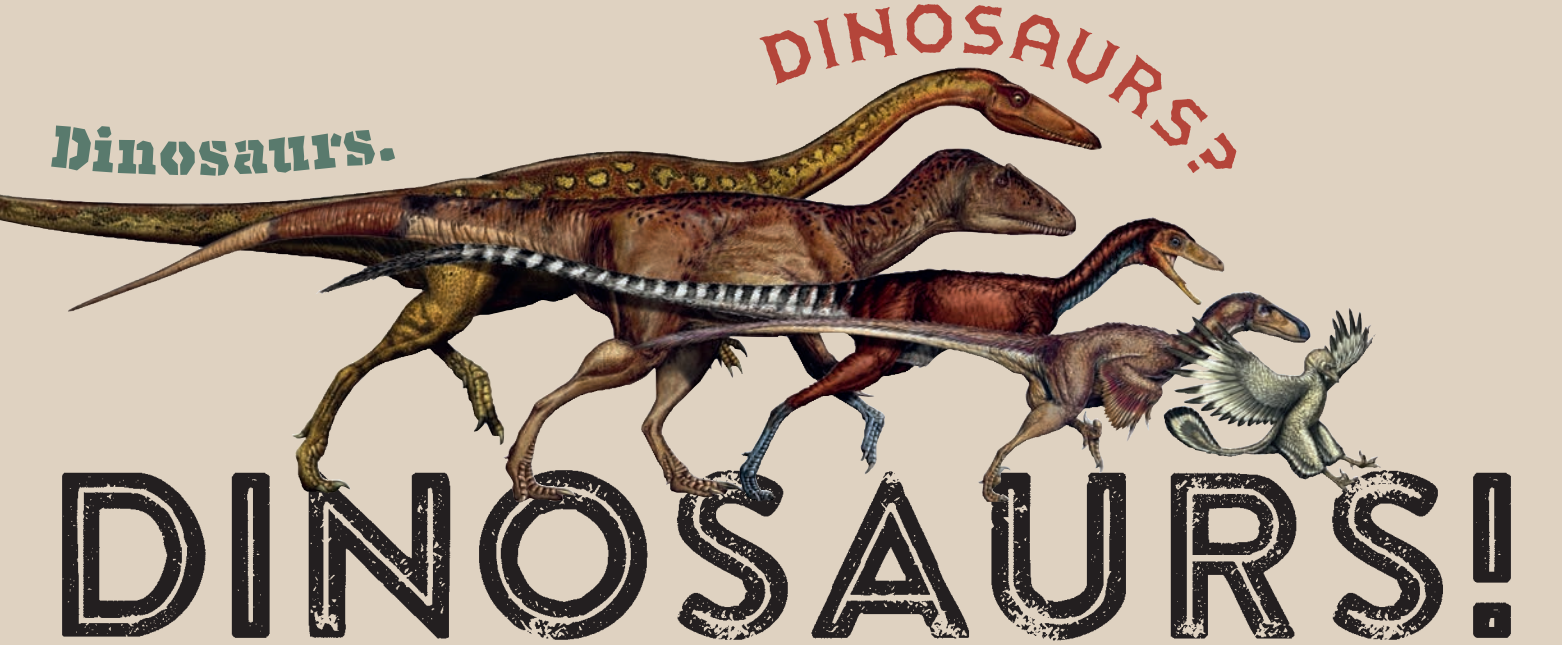
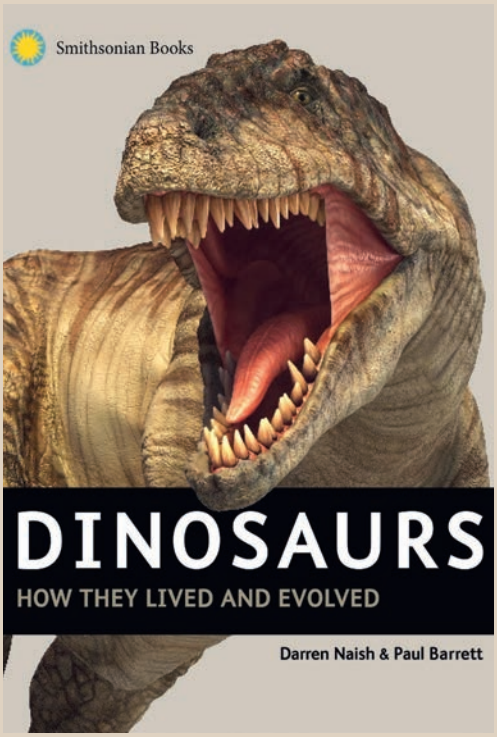
NOVEMBER 2016

ENTANGLED BLACK HOLES

The obscure quantum phenomenon offers tantalizing clues to the nature of spacetime

INSIDE



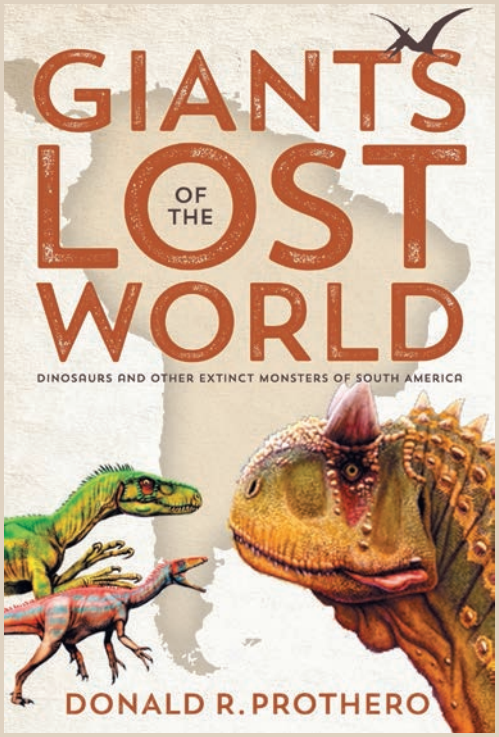


Dinosaurs

Darren Naish and Paul Barrett

HC, 9781588345820, $29.95

A stunning overview of dinosaurs, emphasizing the latest paleontological developments from around the world and providing insight into how these incredible creatures lived and evolved.

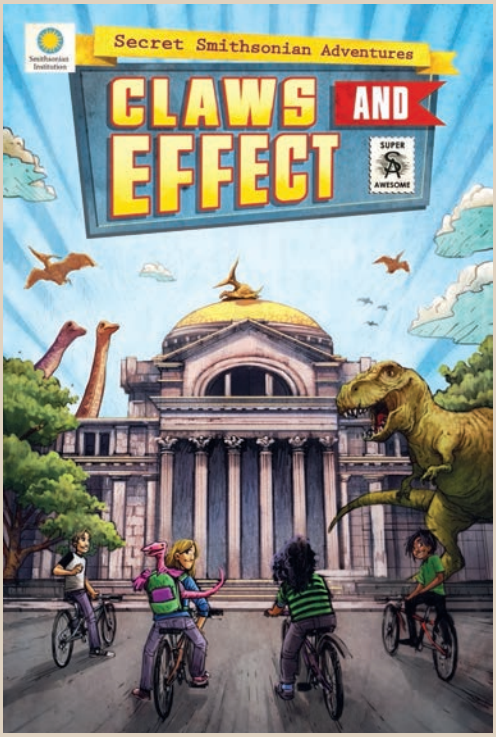


Giants of the Lost World

Donald R. Prothero

HC, 9781588345738, $27.95

"Delivers amusing anecdotes, a lucid history of evolutionary ideas, stories of the great fossil discoveries, and an entertaining description of animal evolution on an isolated continent."
-Kirkus Reviews



Claws and Effect

Kientz et al.

PB, 9781588345677, $10.95

In this exciting second graphic novel in the *Secret Smithsonian Adventures* series, four middle-schoolers use their Smithsonian smarts to battle attempts to bring dinosaurs back to life – for profit!

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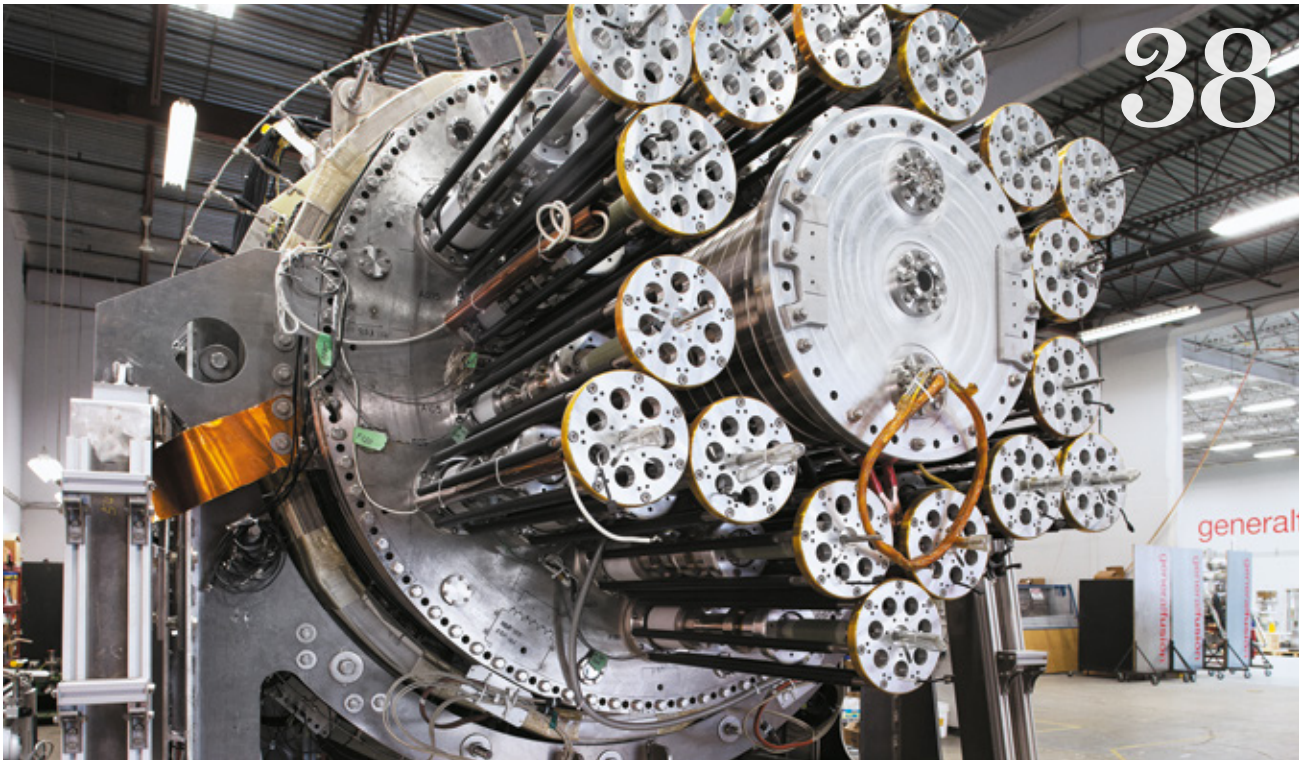

ON THE COVER
If two distant black holes were to become entangled, physicists have realized, they may produce a wormhole bridging two separate regions of spacetime. This connection between entanglement and wormholes could help reveal the quantum nature of spacetime. Illustration by Malcolm Godwin, Moonrunner Design.

Photograph by Chris Mueller

SCIENTIFIC AMERICAN

9

11

76

ON THE WEB

Antibiotic Resistance
Scientific American covers the United Nations summit addressing the global threat of superbugs.
Go to www.ScientificAmerican.com/nov2016/superbugs

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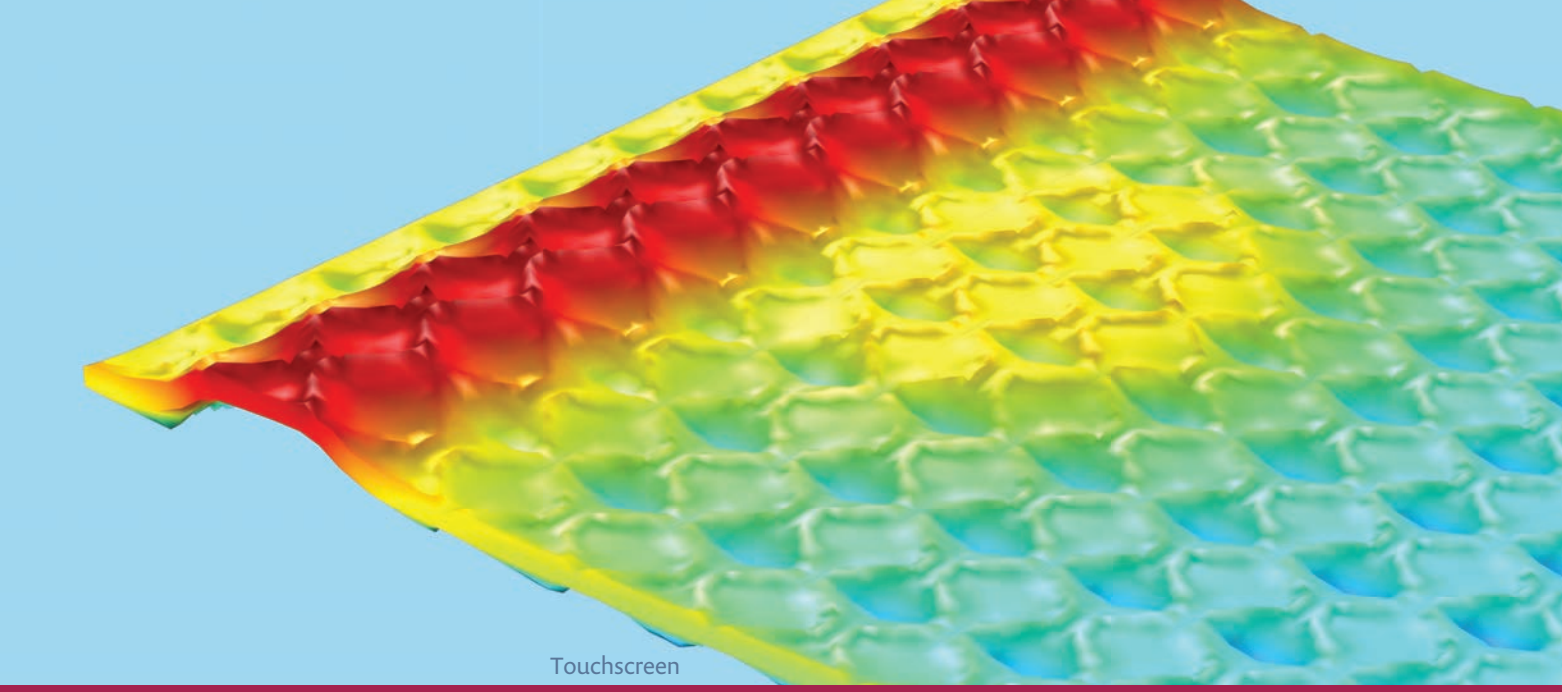

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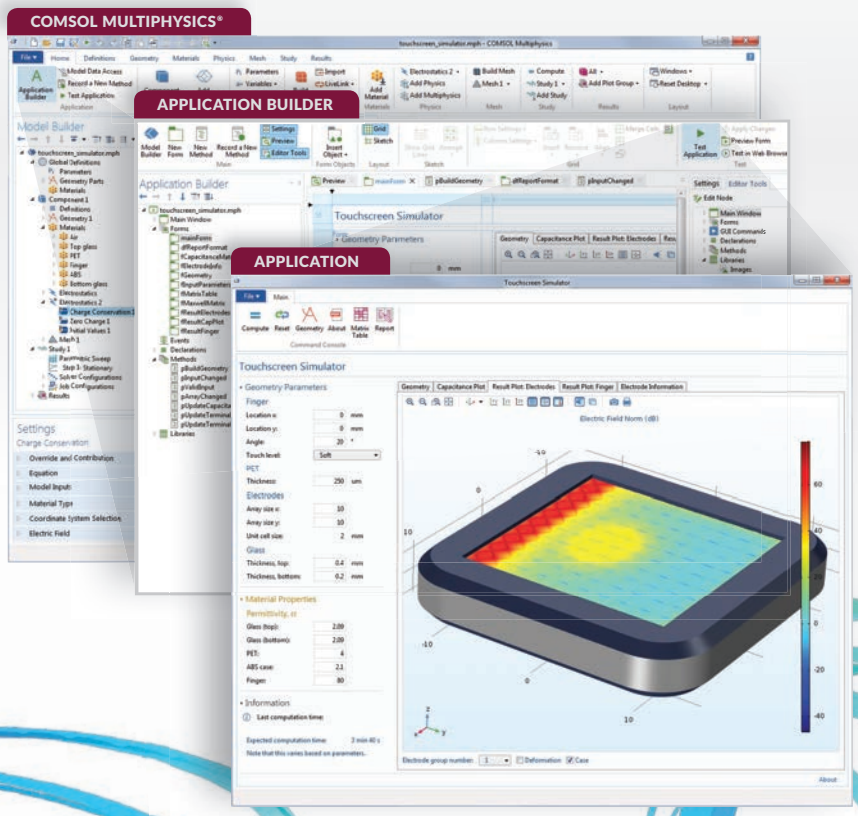

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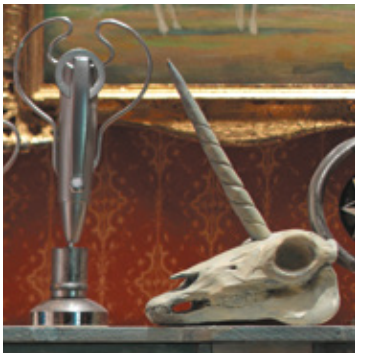
Mariette DiChristina is editor in chief of *Scientific American*. Follow her on Twitter @mdichristina

Theory and Truth

In 1935 Albert Einstein and his collaborators wrote two papers about what seemed to be vastly different things. One, which he famously later described uncomfortably as "spooky action at a distance," is quantum entanglement: a surprising connection between objects, such as atoms or subatomic particles, which may be quite far apart. The other is wormholes, shortcuts between distant regions of space and time predicted by relativity.

Work by theorists, including Juan Maldacena, author of this issue's cover story, "Black Holes, Wormholes and the Secrets of Quantum Spacetime," suggests a surprising link between the two phenomena. As he writes, "quantum mechanics' entanglement and general relativity's wormholes may actually be equivalent"—with profound implications, including the tantalizing possibility of someday developing a unified theory of quantum mechanics and spacetime. Turn to page 26 for a brain-bending exploration at the edges of physics.



UNICORN HORN, if only it existed, might be useful for piercing dangerous fallacies about science.

Not every area of science is in the realm of the theoretical, where we might debate the veracity of a particular field of inquiry and its possible ultimate outcomes. In many areas of perhaps more mundane human endeavor, we *know* what the truth looks like, thanks to uncounted numbers of experimentalists who have provided evidence-based documentation in thousands of studies conducted over decades or longer. Still, some will deny the data.

In an election year, with so many candidates rejecting even basic truths, it seems especially appropriate to fulfill a promise that *Scientific American* made to readers in its first issue, in 1845: "In conducting this publication we shall endeavor to avoid all expressions of sentiment, on any sectional, sectarian, or political party subject; but we shall exercise a full share of independence, in the occasional exposure of ignorance and knavery."

With this in mind, we offer "5 Things We Know to Be True," starting on page 46. In a series of essays, our expert authors describe areas where research is definitive: that the process of evolution explains life as we know it today, that human-caused climate change is real, that vaccines do not cause autism, that homeopathy is bunk and that aliens have not, in fact, visited our blue planet. The package calls out numerous other fallacies, some entertaining and some distressing.

As Einstein himself wrote in his *Scientific American* article, "On the Generalized Theory of Gravitation," in April 1950, "experience alone can decide on truth." Here's hoping that more people can come to embrace that experience along with an evidence-based view of the world. SA

Illustration by Red Nose Studio (unicorn), Illustration by Nick Higgins (DiChristina)

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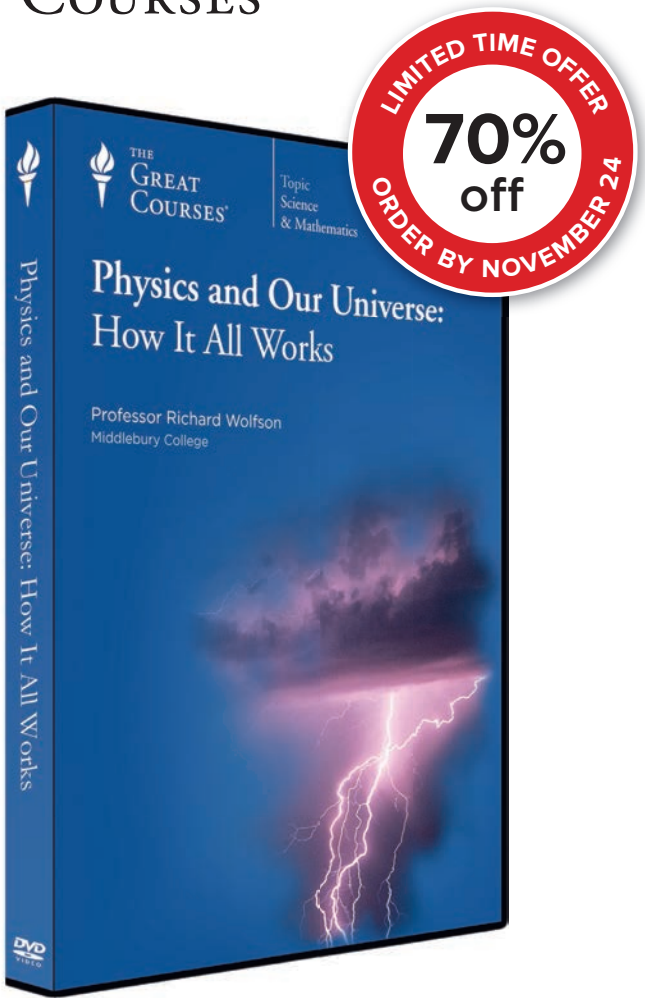

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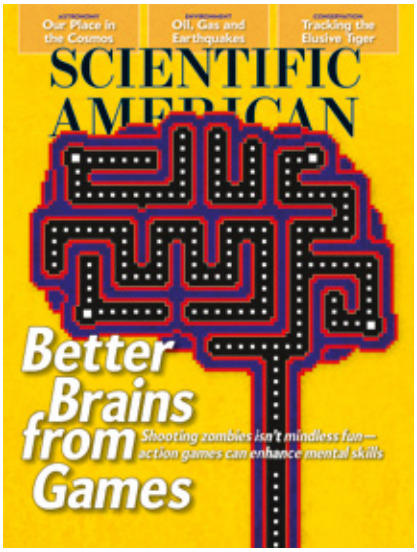

July 2016

DISTANT STARSHADE

In "How to Find Another Earth" [Advances], Lee Billings reports on NASA's Wide-Field Infrared Survey Telescope (WFIRST) and a "starshade" that the agency is considering using to help it image other Earths. Billings describes the two as tens of thousands of kilometers apart. Their desired relative positions are a matter of calculations that, by now, may be almost routine. But *maintaining* the precise relative positions of objects so far apart must be a daunting requirement. Has this been worked out?

KEN KNOWLTON
Sarasota, Fla.

BILLINGS REPLIES: Indeed, formation flying would be crucial for any telescope hoping to make use of a starshade. It is already routine in space, notably in rendezvous maneuvers of spacecraft arriving at the International Space Station (ISS). Controlling the starshade and telescope to achieve formation flying is not thought to be a technological challenge—it would require that each spacecraft control its position with an accuracy of about one meter, whereas a spacecraft docking with the ISS must control its position to better than 30 centimeters. Instead the challenge is in sensing the lateral motions of the two far-separated spacecraft, which would each register as milliarcsecond shifts in position on the sky relative to the other. A telescope with a fine-guidance camera like that of the Hubble Space Telescope could detect the precise lateral position of a starshade bearing an LED bank and a laser beacon. Distances between the two spacecraft would be easily measured via radio transponders.

"I don't doubt that computer games improve some cognitive skills. The problem is that they appear to be replacing every other childhood activity."

LAKE MCCLENNEY *FALLBROOK, CALIF.*

BRAIN GAMES

When doing research with human subjects, the control group is crucial. In "The Brain-Boosting Power of Video Games," Daphne Bavelier and C. Shawn Green describe how they used participation in a "social game" to compare with their treatment: participation in a computer action game. If those are the only two choices, their results are trivial.

What about comparing participation in computer games with equal time in such activities as playing tennis, building a fort, cooking dinner or even reading a book? I don't doubt that computer games improve some cognitive skills. The problem is that they appear to be replacing every other childhood activity. And comparing the effects of participation in one kind of game with another isn't useful science, although I'm sure it makes the CEOs of the game corporations very happy.

LAKE MCCLENNEY
Fallbrook, Calif.

TWO LEGS BETTER?

Reading through John Pavlus's article "Bipedal Metal," I can find no explanation of why a robot should have two legs (apart from possible application to human prostheses) like the ones he reports on. It seems that a three- or four-legged robot would be more stable and better able to negotiate rough terrain. And there is no reason why it couldn't have just one arm. Are we following the pattern of science-fiction writers who assumed an alien creature would follow the contingent human body type?

MICHAEL I. SOBEL
Professor emeritus of physics
Brooklyn College

PAVLUS REPLIES: According to the researchers I interviewed, a big reason to design "anthropomorphic" bipedal robots is to optimize their versatility and agility in human-built environments. These environments are already built to accommodate a two-armed, two-legged body, and so a robot with the same body could, ideally, exploit those same advantages. A three-legged, one-armed robot might have difficulty navigating built environments efficiently. Several of the teams in the 2015 DARPA Robotics Challenge did build highly capable nonbipedal robots, but the hope is that an effective bipedal robot would be able to do everything those unusually shaped robots did and more.

LANIAKEA SUPERCLUSTER

I was astonished and exasperated in almost equal measures by "Our Place in the Cosmos," Noam I. Libeskind and R. Brent Tully's article on the Laniakea supercluster of galaxies, which includes the Milky Way. Astonished by the scale and beauty but frustrated because the authors discuss methods for determining the galaxies' radial peculiar velocities (those relative to their motion from cosmic expansion), but they give no hint of how they estimate the galaxies' transverse velocities (those perpendicular to the line of sight). Without knowing the latter, we have no way of appreciating how reliable the conclusions they draw are.

PAUL FRIEDLANDER
London

LIBESKIND REPLIES: There is no way to measure the transverse velocity of anything but the closest galaxies (and even then it is exceedingly difficult). That's because that velocity is simply imperceptible, given the huge distances that most galaxies are at. But we can estimate it based on our reconstruction methods. What we have to start with is a (relatively speaking)

fairly small sampling of the radial peculiar velocity for some (random) set of galaxies. This set is an incomplete sampling of the galaxies in the heavens because we can't compute the peculiar velocity for all galaxies. Many galaxies don't have the required stars or other markers needed to compute distances. Based on the velocities we do have, we can then find the full 3-D velocity field, which is most consistent with the one-dimensional radial peculiar velocity field we measured. This "guess" also provides us with an estimate for the full 3-D density field, which takes care of the incompleteness of our sampling.

Although this technique sounds dodgy, it actually is not. We can test it by simulating the universe, using well-established techniques, and then "observing" our simulations in the same way we observe the universe, namely by obscuring regions and introducing measurement errors, poor sampling, and so on. We can then apply our suite of techniques and see how well we do. In the simulation, we have the benefit of being able to know the "real" velocities and compare them with the calculated ones. Turns out it works pretty well.

LEAD EXPOSURE

Ellen Ruppel Shell's article on "Gauging the Effects of Lead" [The Science of Health] brings some calm scientific perspective to the discussion on the effects of low-level lead exposure and the means by which blood-level standards are set. I lived nearly my entire childhood a few miles downwind of a lead smelter. My personal observation, though clearly not a scientific study, is that my exposed peers and I have developed normally. I am not suggesting that lead exposure shouldn't be avoided or mitigated but that there is a substantial adult population with similar childhood conditions who should be studied.

Even without precise blood-level measurements, reasonable estimates of these exposures could be made from residual soil levels, production records, exposure levels from smelters operating in developing countries and other sources. Studies checking for the possible effects in such exposed populations could provide a wealth of data.

BERNARD STEBLAY
Lakewood, Colo.

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Donald Trump's Campaign for Science Illiteracy

His statements show a disregard for science that is alarming in a candidate for high office

By the Editors

One of the major-party presidential candidates has had plenty to say during this year's campaign. But almost none of the words from Donald J. Trump have been about the importance of science and science literacy to the nation's economic growth, security and international prestige—as well as to the health and well-being of the American people and the future of the planet itself. Trump has, however, made statements about science over the years, many of them in the form of tweets. They betray his beliefs about scientific issues, so we are reprinting a selection of them here. We have not fact-checked them. SA

CLIMATE CHANGE

The concept of global warming was created by and for the Chinese in order to make U.S. manufacturing non-competitive.

This very expensive GLOBAL WARMING bullshit has got to stop. Our planet is freezing, record low temps, and our GW scientists are stuck in ice

NBC News just called it the great freeze—coldest weather in years. Is our country still spending money on the GLOBAL WARMING HOAX?

Any and all weather events are used by the GLOBAL WARMING HOAXSTERS to justify higher taxes to save our planet! They don't believe it $$$$!

Global warming is based on faulty science and manipulated data which is proven by the emails that were leaked

Ice storm rolls from Texas to Tennessee—I'm in Los Angeles and it's freezing. Global warming is a total, and very expensive, hoax!

THE AUTISM-VACCINE CONNECTION

I've seen people where they have a perfectly healthy child, and they go for the vaccinations, and a month later the child is no longer healthy.

Autism rates through the roof—why doesn't the Obama administration do something about doctor-inflicted autism. We lose nothing to try.

Healthy young child goes to doctor, gets pumped with massive shot of many vaccines, doesn't feel good and changes—AUTISM. Many such cases!

EBOLA

The U.S. cannot allow EBOLA infected people back. People that go to far away places to help out are great—but must suffer the consequences!

Same CDC which is bringing Ebola to US misplaced samples of anthrax earlier this year http://www.cnn.com/2014/07/15/health/cdc-anthrax-ziploc-bags/… Be careful.

HEALTH CARE

ObamaCare gives free insurance to illegal immigrants. Yet @BarackObama is cutting our troops healthcare. http://bit.ly/xFlfQs Outrageous.

Obama is going to take away over 90M Americans' healthcare plans but he is letting Iran keep its nukes. Just think about that.

OTHER TOPICS

Fracking poses ZERO health risks http://bit.ly/18pdO8H In fact, it increases our national security by making us energy independent.

It would be nice if our commander-in-chief was as concerned for our Veterans health as he is for illegal immigrants becoming citizens.

Not only are wind farms disgusting looking, but even worse they are bad for people's health http://bit.ly/I9Dl8k They should be outlawed and allowed only in heavily industrialized areas.

Seems to be the next election must be about jobs and gas prices—not birth control.

Remember, new "environment friendly" lightbulbs can cause cancer. Be careful—the idiots who came up with this stuff don't care.

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Illustration by Steve Brodner


Leana S. Wen is the Baltimore City health commissioner. She is an emergency physician and co-author of the book *When Doctors Don't Listen: How to Avoid Misdiagnoses and Unnecessary Tests* (St. Martin's Press, 2012). **M. Cooper Lloyd** is a resident physician in internal medicine and pediatrics at the Johns Hopkins Hospital and former special assistant to the commissioner at the Baltimore City Health Department.

Attacking the Roots of Violence

By treating it as a public health problem, Baltimore is saving lives

By Leana S. Wen and M. Cooper Lloyd

In Baltimore, violence has become a near-daily occurrence. In 2015, for example, this city of more than 620,000 people saw 344 homicides. But by tackling violence as a public health issue, Baltimore is forging a new model for how to keep citizens safe.

In 2007 the city launched its Safe Streets program, modeled after the Cure Violence program in Chicago. Targeting high-risk youth, Safe Streets hires "violence interrupters" to mediate conflict before it has the chance to escalate into violence. These interrupters have often been incarcerated themselves in the past, which brings credibility and experience to their work on the streets.

In 2014 Safe Streets workers had 15,000 encounters with the public and mediated 880 conflicts, more than 80 percent of which were deemed to be likely or very likely to result in gun violence. Three of four program sites saw significant reductions in gun violence; homicides dropped by 56 percent in one neighborhood and by 26 percent in another. Surveys show that people in the program were significantly less likely to find it acceptable to use a gun to settle a conflict, compared with peers in other neighborhoods that did not have the program.

This year Safe Streets will expand to several Baltimore hospitals, where interrupters will help victims of violence—who are themselves often participants in dangerous conflicts—address the trauma they have experienced and navigate reentry into their communities. Although studies to date are small, evidence suggests that people enrolled in this kind of program are three times less likely to be arrested for a violent crime in the future.

But Baltimore's efforts go even further by dealing with factors that contribute to conflict—starting with one of its greatest contributors: addiction. More than 80 percent of individuals in jails have used illegal substances, and more than 30 percent were under the influence of drugs at the time of their offense.

Over the past year Baltimore has led one of the most aggressive opioid overdose prevention campaigns in the country. In October 2015 the Baltimore City Health Department declared overdose to be a public health emergency and issued a blanket prescription for naloxone—the lifesaving drug that reverses the lethal effects of opioids—for every one of the city's residents. The health department trained more than 8,000 people to use naloxone in 2015—in jails, public housing, bus shelters, street corners and markets.

The focus on preventing overdose is combined with a citywide commitment to better access to quality, on-demand drug treatment services and long-term recovery support. Recovery requires medication-assisted treatment, psychological support and wraparound services, which get teachers, clergy and other community members involved in supporting drug abusers. The health department has started a 24/7 hotline that connects people to mental health and substance abuse treatment. It has also launched a public education campaign, "Don't Die," to educate citizens about overdose.

But intervening on the front end does not stop at addiction; the roots of violence often begin much earlier, in inequalities that have been present from early childhood and even birth. A decade ago the city's infant health ranked among the poorest in the country, with enormous disparities between black and white birth outcomes. In response, the health department led the creation of an evidence-based initiative, B'More for Healthy Babies, that offers extensive support services to mothers and that sends nurses and counselors on home visits to low-income families. The results have been extraordinary: within seven years infant mortality decreased by 28 percent to its lowest in Baltimore's history, the teen birth rate decreased by 36 percent, and the disparity between black and white infant deaths decreased by almost 40 percent.

Violence does not happen randomly or in isolation. It is one tragic, final result of inequities that continually build if left unaddressed. By treating it as a public health issue, it can be prevented—and, perhaps one day, even cured. SA

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Illustration by Taylor Callery

Veterinarians perform a health checkup on a young deer on the Yamal Peninsula in Siberia after an anthrax outbreak there.

RUSSIAN EMERGENCY MINISTRY *AFP Photo*

CLIMATE CHANGE

What Lies Beneath

Larger portions of Earth's permafrost are thawing, unleashing trapped microorganisms into the environment

This past summer anthrax killed a 12-year-old boy in a remote part of Siberia. At least 20 other people, also from the Yamal Peninsula, were diagnosed with the potentially deadly disease after approximately 100 suspected cases were hospitalized. Additionally, more than 2,300 reindeer in the area died from the infection. The likely cause? Thawing permafrost. According to Russian officials, thawed permafrost—a permanently frozen layer of soil—released previously immobile spores of *Bacillus anthracis* into nearby water and soil and then into the food supply. The outbreak was the region's first in 75 years.

Researchers have predicted for years that one of the effects of global warming could be that whatever is frozen in permafrost—such as ancient bacteria—might be released as temperatures climb. This could include infectious agents humans might not be prepared for, or have immunity to, the scientists said. Now they are witnessing the theoretical turning into reality: infectious microorganisms emerging from a deep freeze.

Although anthrax occurs naturally in all soil and outbreaks unrelated to permafrost can occur, extensive permafrost thaw could increase the number of people exposed to anthrax bacteria. In a 2011 paper published in *Global Health Action,* co-authors Boris A. Revich and Marina A. Podolnaya wrote of their predictions: "As a consequence of permafrost melting, the vectors of deadly infections of the 18th and 19th cen-

INSIDE

turies may come back, especially near the cemeteries where the victims of these infections were buried."

And permafrost is indeed thawing—at higher latitudes and to greater depths than ever before. In various parts of Siberia the active layer above permafrost can thaw to a depth of 50 centimeters every summer. This summer, however, there was a heat wave in the region, and temperatures hovered around 35 degrees Celsius—25 degrees warmer than usual. The difference possibly expanded or deepened the thaw and mobilized microorganisms usually stuck in rigid earth. Although scientists have yet to calculate the final depth, they postulate that it is a number that has not been seen in almost a century. Permafrost thaw overall could become widespread with temperatures only slightly higher than those at present, according to a 2013 study in *Science*. Heat waves in higher latitudes are becoming more frequent as well.

What thawing permafrost could unleash depends on the heartiness of the infectious agent involved. A lot of microorganisms cannot survive in extreme cold, but some can withstand it for many years. "*B. anthracis* are special because they are sporulating bacteria," says Jean-Michel Claverie, head of the Mediterranean Institute of Microbiology and a professor at Aix-Marseille University in France. "Spores are extremely resistant and, like seeds, can survive for longer than a century."

Viruses could also survive for lengthy periods. In 2014 and 2015 Claverie and his colleague Chantal Abergel published their findings on two still infectious viruses from a chunk of 30,000-year-old Siberian permafrost. Although *Pithovirus sibericum* and *Mollivirus sibericum* can infect only amoebas, the discovery is an indication that viruses that infect humans—such as smallpox and the Spanish flu—could potentially be preserved in permafrost.

Human viruses from even further back could also make a showing. For instance, the microorganisms living on and within the early humans who populated the Arctic could still be frozen in the soil. "There are hints that Neandertals and Denisovans could have settled in northern Siberia [and] were plagued by various viral diseases, some of which we know, like smallpox, and some others that might have disappeared," Claverie says. "The fact that there might be an infection continuity between us and ancient hominins is fascinating—and might be worrying."

Janet Jansson, who studies permafrost at the Pacific Northwest National Laboratory in Washington State, is not worried about ancient viruses. Several attempts to discover these infectious agents in corpses have come up empty, she notes. She does advocate, however, for further research to identify the wide range of permafrost-dwelling organisms, some of which could pose health risks. To accomplish that goal, she and others are using modern molecular tools—such as DNA sequencing and protein analysis—to categorize the properties of unknown microorganisms, sometimes referred to as microbial dark matter.

The likelihood and frequency of outbreaks similar to the one in Siberia will depend on the speed and trajectory of climate change. For instance, it is possible that another heat wave will expose the carcasses of animals infected by anthrax, Revich says. "The situation on the Yamal Peninsula has shown that the risk of the spread of anthrax is already real," he adds.

In effect, infectious agents buried in the permafrost are unknowable and unpredictable in their timing and ferocity. Thus, researchers say thawing permafrost is not our biggest worry when it comes to infectious diseases and global warming. The more immediate, and certain, threat to humans is the widening geographical ranges of modern infectious diseases (and their carriers, such as mosquitoes) as the earth warms. "We now have dengue in southern parts of Texas," says George C. Stewart, McKee Professor of Microbial Pathogenesis and chair of the department of veterinary pathobiology at the University of Missouri. "Malaria is seen at higher elevations and latitudes as temperatures climb. And the cholera agent, *Vibrio cholerae,* replicates better at higher temperatures."

Unlike the zombie microbes lurking in the permafrost, modern spreading diseases are more of a known quantity, and there are proved ways to curb them: mapping trends, eliminating mosquito-breeding sites and spraying insecticides. Of course, dramatically lowering fossil-fuel emissions to combat climate change could tackle both threats—the resurgence of ancient and deadly pathogens and the widening ranges of infectious diseases—in one shot. —*Sara Goudarzi*

BIOLOGY

Tension in Taxonomy

A debate rages between DNA bar coders and traditional taxonomists over how to classify species

A couple of months ago beetles were demoted. Biologists had long thought these insects were life's most diverse order, but according to a new study in *Philosophical Transactions of the Royal Society B,* that honor now goes to flies. The finding has led to tension within the taxonomy community—part of an ongoing debate about how to define a species.

The fly's new designation took place after scientists at the University of Guelph in Ontario analyzed more than one million insects using DNA bar coding, a computerized taxonomic method that identifies a genetic profile from a bit of an organism's DNA. That profile is then given a bar-code index number, or BIN, which represents a species. The scientists found that one family of flies had 16,000 BINs, a 10-fold increase from previous estimates. If extrapolated worldwide, this finding could "reverse a long-held view of what life is like on our planet," says lead author Paul D. N. Hebert.

But many traditional taxonomists disagree with the idea that a BIN is equivalent to a species. This paper "highlights a truly fundamental difference in how they categorize biodiversity, such that their numbers and ours can differ by more than an order of magnitude," says Doug Yanega, an entomologist and traditionalist at the University of California, Riverside. "That's a really astonishing scale of difference. It's like we're looking at different planets."

The traditionalists, who largely classify species by examining and comparing physical specimens, argue that bar coding can help place organisms in taxonomic orders and families but that it lacks the resolution for categorizing species on its own. In fact, the taxonomy community has already embraced molecular phylogeny, which often uses DNA to figure out evolutionary relationships. "DNA bar coding is not a substitute for traditional taxonomy," says Andrew V. Z. Brower, a professor of biology at Middle Tennessee State University. "All it does is flag problems that need to be investigated by taxonomists."

> "It's like we're looking at different planets."—Doug Yanega *University of California, Riverside*

Still, bar coders—a small but influential group in the field—say the method is accurate and point to studies in which the number of species determined by DNA bar coding matches prior counts. Such is the case with European beetles. Some scientists have also embraced the technology because it allows huge volumes of DNA to be analyzed quickly and cheaply, dramatically increasing knowledge about biodiversity at a time when human activities imminently threaten still undiscovered species. "We can't afford to wait [for traditional taxonomic methods]," Hebert says. "We're at a big risk of burning the book of life before we even read it."

The overall consensus is that bar coding has raised legitimate questions. But many taxonomists remain reluctant to correlate BINs to individual species until the technology is refined further. "It's a powerful tool for assessing a big biodiversity picture, but when you see DNA bar codes as species, you run into problems," says DeeAnn Reeder, a biologist at Bucknell University. "Bar coding is still a brave new world." For now, perhaps the only certain things in this debate are death and taxa. —*Kat Long*

Illustrations by Thomas Fuchs

HEALTH

The Artificial Pancreas Gets Real

Devices that autonomously regulate blood sugar levels are nearing reality

Type 1 diabetics, who do not produce the hormone insulin, must be vigilant about their blood glucose (sugar) levels. Chronic high blood sugar, which results from too little insulin, can lead to nerve and organ damage; low levels can cause seizures or death. The current gold standard in care involves a continuous glucose monitor (a sensor inserted under the skin), an insulin pump (a wearable device that can be programmed to release varying amounts of insulin), and a lot of trial-and-error work by the user—because the monitor and the pump don't talk to each other.

Researchers have been working to make things easier for patients by integrating and automating the steps in the process. The end result—the artificial pancreas—is a system that can figure out how much insulin the body needs in near real time and then deliver that amount on its own. "The artificial pancreas will allow us to live a near-normal life until there is a cure," says Kelly Dunkling Reilly, a registered nurse and certified diabetes educator who was a subject in a recent clinical trial of Boston-based Beta Bionics's iLet pancreas. "For the first time in my 24 years with diabetes, I was able to exercise whenever I wanted and work with my patients without the constant fear of hypoglycemia." After more than a decade in development, several artificial pancreas projects are moving into the final stages before they become widely available.

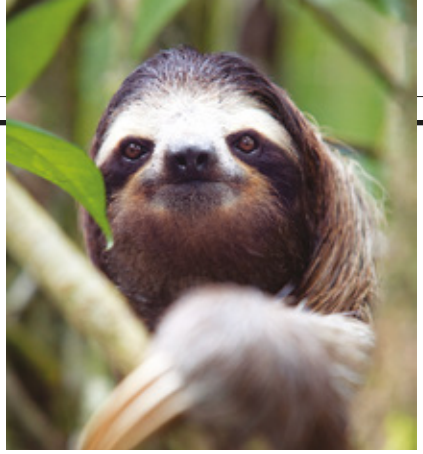
—*Ellen Sheng*

1. In June medical device maker Medtronic filed a premarket-approval application to the Food and Drug Administration for a "hybrid closed loop"—an insulin pump that analyzes data from a continuous glucose monitor and automatically adjusts insulin rates. Users would still need to input insulin doses to account for meals. A study that followed 124 diabetic participants using the Medtronic device wrapped up in May and showed that the system was safe and could be trusted to autonomously determine doses.

2. One of the largest clinical trials so far kicked off at the start of this year with 240 patients based throughout the U.S. and Europe. Led by researchers at the University of Virginia and Harvard University, along with a consortium of organizations, the trial will test the safety and effectiveness of a system that integrates an insulin pump, a continuous glucose monitor and a smartphone. The smartphone relies on an algorithm to analyze blood sugar readings and then instructs the pump on how much insulin to release. Two different algorithms will be tested.

3. Beta Bionics is working on a device (*left*) that administers both insulin and glucagon, the hormone that raises blood sugar. With data from a continuous glucose monitor, its algorithm decides which hormone to release and how much. "Using both insulin and glucagon allows for tighter control of blood sugar levels," CEO Edward Damiano says. He hopes to start clinical trials in mid-2017. An insulin-only version could receive approval as early as 2018.

COURTESY OF BETA BIONICS, INC.



RAÚL BARRERO *Getty Images*

ANIMAL BEHAVIOR

Laziness: An Evolutionary Trait

A serene lifestyle and the ability to modify body temperature make sloths the masters of slow

After seven years of studying three-toed sloths, scientists at the University of Wisconsin–Madison have made it official: the tree-dwelling animals are the slowest mammals on earth, metabolically speaking. "We expected them to have low metabolic rates, but we found them to have *tremendously* low energy needs," says ecologist Jonathan Pauli.

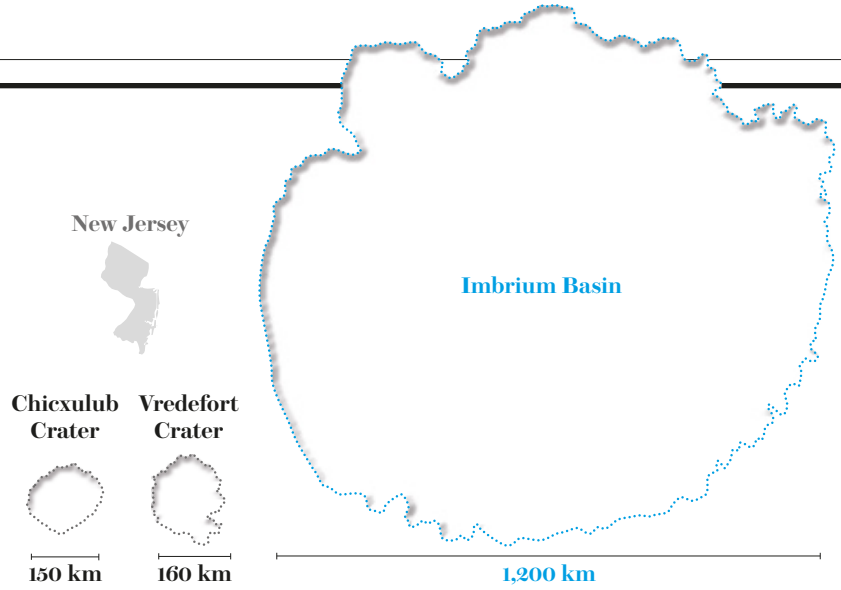
To reach this conclusion, Pauli and his colleague M. Zachariah Peery measured the metabolic rates of 10 three-toed sloths and 12 of the two-toed variety in Costa Rica and compared the results with similar studies of 19 other species of leaf-eating mammals. With a metabolic rate of 162 kilojoules per day per kilogram, the three-toed sloths have lower energy needs than koalas, which require 410 kilojoules per day per kilogram. Two-toed sloths, meanwhile, have an energetic expenditure of 234. Giant pandas are the only contenders that come close to the title of slowest mammal—at 185 kilojoules.

According to the study, published in August in *American Naturalist,* there is a suite of behavioral, physiological and anatomical adaptations that allow sloths to lead minimally exerting lives in the jungle canopies of Central and South America. For example, they have small home ranges and spend most of their time eating, resting or sleeping. They also have the rare ability to adjust their internal thermostat. "They're slightly heterothermic, so they can fluctuate their body temperature by about five degrees Celsius to be in line with the outside temperature. By relaxing their body temperature, they have big savings in terms of energetic output," Pauli explains. Who said sloth was a deadly sin? —*Eduardo Garcia*

SPACE

Lunar Landscaping

The Man in the Moon has an enormous right eye: the crater known as the Imbrium Basin, which is 1,200 kilometers across. The cavity was created roughly four billion years ago during a collision with something big. How big? "About the size of New Jersey," says Peter H. Schultz, a planetary geoscientist at Brown University who published a new estimate of the object's heft in *Nature*. To figure out the impactor's dimensions, Schultz and his colleague David A. Crawford turned to the surface features of the moon—in particular the grooves that emanate from the collision site, which were carved by flying chunks of the impactor. The researchers used measurements of those grooves and laboratory experiments to calculate the rock's size, speed and impact angle. The updated magnitude is 10 times more massive than previous estimates, which were based on computer simulations, and is a reminder of how little we know about the early solar system, Schultz says. —*Karl J. P. Smith*



BY THE NUMBERS

10 kilometers
Estimated diameter of the Chicxulub impactor, which struck modern-day Mexico approximately 66 million years ago and contributed to the demise of the dinosaurs.

10 kilometers
Estimated diameter of the asteroid that formed South Africa's Vredefort Crater, the largest confirmed crater on Earth's surface.

250 kilometers
Newly estimated diameter of the asteroid that created the moon's Imbrium Basin.

Graphic by Amanda Montañez

SOURCES: "ORIGIN AND IMPLICATIONS OF NON-RADIAL IMBRIUM SCULPTURE ON THE MOON," BY PETER H. SCHULTZ AND DAVID A. CRAWFORD, IN *NATURE*, VOL. 535; JULY 21, 2016 (*Imbrium Basin outline and asteroid diameter*); "THE CHICXULUB ASTEROID IMPACT AND MASS EXTINCTION AT THE CRETACEOUS-PALEOGENE BOUNDARY," BY PETER SCHULTZ ET AL., IN *SCIENCE*, VOL. 327; MARCH 5, 2010 (*Chicxulub impactor diameter*); "CONSTRAINTS ON THE SIZE OF THE VREDEFORT IMPACT CRATER FROM NUMERICAL MODELING," BY E. P. TURTLE AND E. PIERAZZO, IN *METEORITICS & PLANETARY SCIENCE*, VOL. 33, NO. 3; MAY 1998 (*Vredefort Crater asteroid diameter*)

PUBLIC HEALTH

Mosquitoes to the Rescue

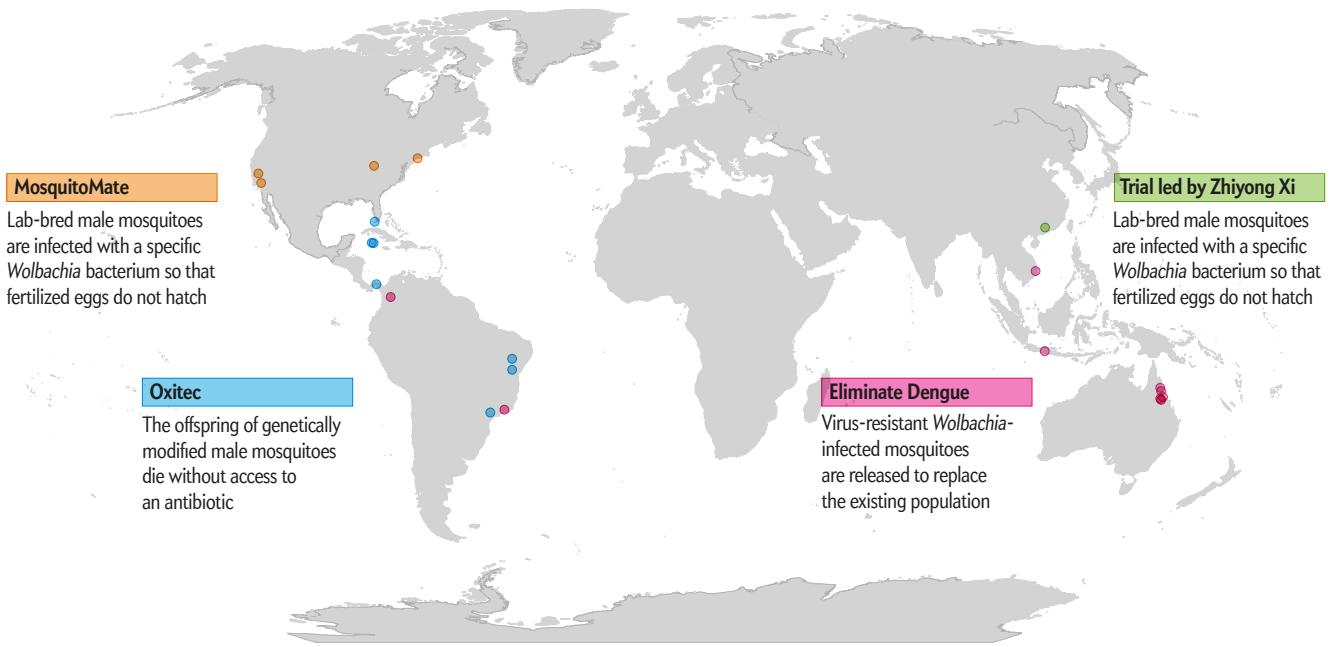
Scientists are turning the infectious bloodsuckers into allies in the global war on disease

This month the first U.S. experiment to release genetically modified (GM) mosquitoes into the wild gets put to a vote in Key Haven, Fla., and the county of Monroe. If the Florida Keys Mosquito Control District then approves the trial, U.K. biotech firm Oxitec will release millions of mutant male mosquitoes that had required an antibiotic to stay alive until adulthood. These males will pass the dependency to their offspring, which will then die without access to the drug. The resulting population plummet could reduce the risk of mosquitoes spreading diseases such as dengue fever—Key Haven suffered an outbreak in 2009–2010—and the growing threat of the Zika virus.

Many in Key Haven have voiced concerns about the safety of hosting GM insects in their backyards, but outside experts say these mosquitoes would be innocuous. "There are no potential [health] risks to the Oxitec genetically modified mosquitoes approach," says Thomas Miller, an emeritus professor of entomology at the University of California, Riverside. And although this would be a first for the U.S., previous Oxitec field trials in other countries have successfully reduced local mosquito populations by more than 90 percent without any indication of worrisome side effects. Indeed, dozens of experiments with altered mosquitoes have taken place over the past five years throughout the world in an effort to squash the spread of mosquito-associated diseases. Keep your friends close and your enemies closer.

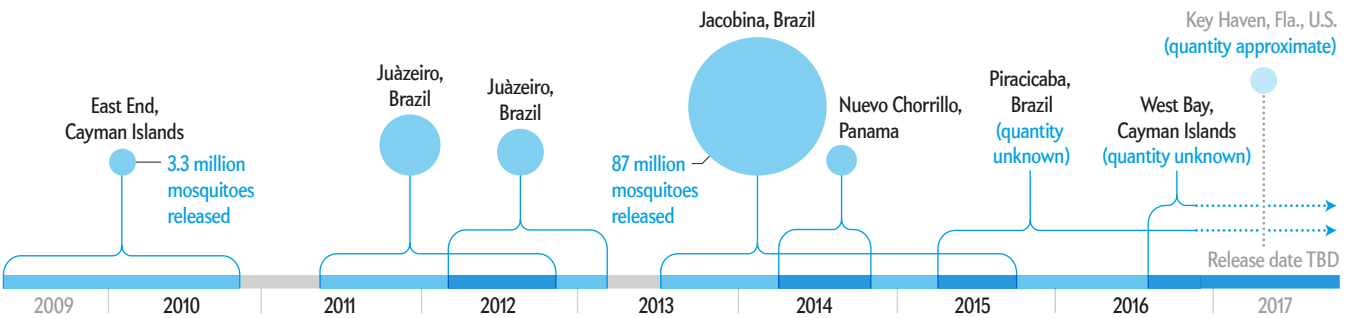
—Jeremy Hsu

Experimental Mosquito Trials around the World



Oxitec's Timeline

The company's planned release of genetically modified mosquitoes in Florida would be the latest of several such trials Oxitec has run since 2009.



WILLIAM VOLCOV Getty Images (mosquito)

Graphic by Amanda Montañez

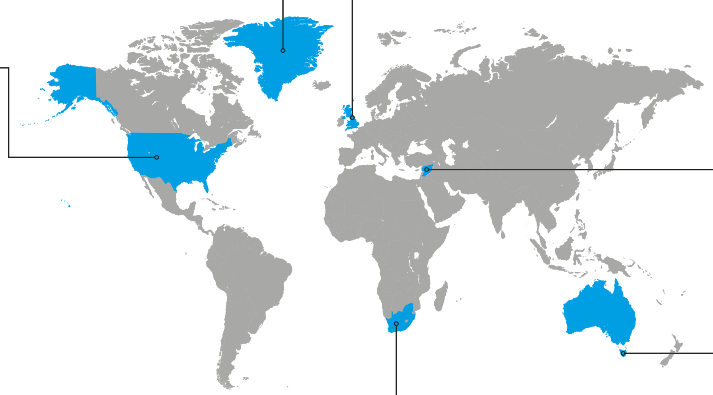
IN THE NEWS

Quick Hits

GREENLAND
Geologists discovered what some think may be the oldest known fossils on earth. The scientists said the objects are 3.7-billion-year-old stromatolites, layered structures created by lime-secreting cyanobacteria.

U.K.
The British government imposed a tax on companies that sell products with added sugar. Proponents hope the levy will help reduce obesity among children.

SYRIA
An analysis of mortality data from 22 countries in the Middle East and northern Africa found that conflict and civil strife have decreased life expectancy across the region. In Syria, for example, the life expectancies of both women and men are now about five years lower than in 2010.

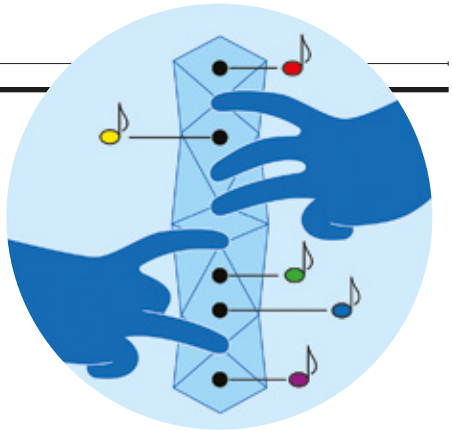


U.S.
The Centers for Disease Control and Prevention announced that the nasal spray form of the flu vaccine does not work. Preliminary research indicated that during the last flu season, the spray was only 3 percent effective in children between the ages of two and 17. The agency now recommends the flu shot for everyone.

AUSTRALIA
Over the past two decades a contagious cancer, called devil facial tumor disease, has reduced the population of Tasmanian devils by more than 80 percent. But new research shows that the animals may be developing resistance to the disease.

SOUTH AFRICA
The first large-scale clinical trial since 2009 of a vaccine against HIV begins this month. The three-year program will include 5,400 people across four sites. Nearly two thirds of the 2.1 million new HIV infections reported worldwide in 2015 were in sub-Saharan Africa.

For more details, visit www.ScientificAmerican.com/nov2016/advances



TECHNOLOGY

Introducing the Acoustic Prism

The device splits sounds without digital help

Nearly four centuries ago Isaac Newton demonstrated that a glass prism could separate white light into all the colors of a rainbow. Now a Switzerland-based team of electrical engineers has built a device that can do something similar for sound—splitting noise into its constituent frequencies by physical means only.

The so-called acoustic prism comprises a 40-centimeter-long hollow aluminum case with a series of 10 holes on its side. Within, flexible polymer membranes divide the case into chambers. These barriers vibrate and transmit sound to neighboring cavities with a delay that depends on a sound wave's frequency. When the delayed waves escape from the holes, they are refracted in different directions so that waves with the lowest frequencies (comparable to red light) can be heard at the end nearest to the source, whereas higher frequencies (comparable to blue light) are refracted farther down the device. "This mimics how a water droplet or glass prism refracts each color of light at different angles," says Hussein Esfahlani, who studies signal processing at the Swiss Federal Institute of Technology in Lausanne. The device's design was recently published in the *Journal of the Acoustical Society of America*.

The prism began as a thought experiment according to Esfahlani, but in practical terms it could be used to separate meaningful frequencies from incoming white noise or to determine precisely where a specific frequency is coming from. "This is a very elegant and efficient way for distinguishing sound frequencies," says Nicholas Fang, a professor of mechanical engineering at the Massachusetts Institute of Technology, who was not involved in the project. —*Knvul Sheikh*

ENVIRONMENT

Home Is Where They Make It

Elephant footprints can teem with life

When you weigh upward of 6,000 kilograms, you tend to make an impression—literally—wherever you go. Such is the case with the African elephant (*Loxodonta africana*), which, according to new research, is a boon for dozens of other, much tinier species.

As elephants walk through the forest or savanna, they leave big footprints behind them—sometimes 30 centimeters deep. These marks then fill with water, creating microhabitats for other forms of life. Researchers at Germany's University of Koblenz-Landau and other institutions analyzed the contents of 30 footprint pools in Uganda. They found that at least 61 different microinvertebrate species from nine different orders had made the pockets of water home, including mites, mayflies, backswimmers, leeches and gastropods. Tadpoles also showed up.

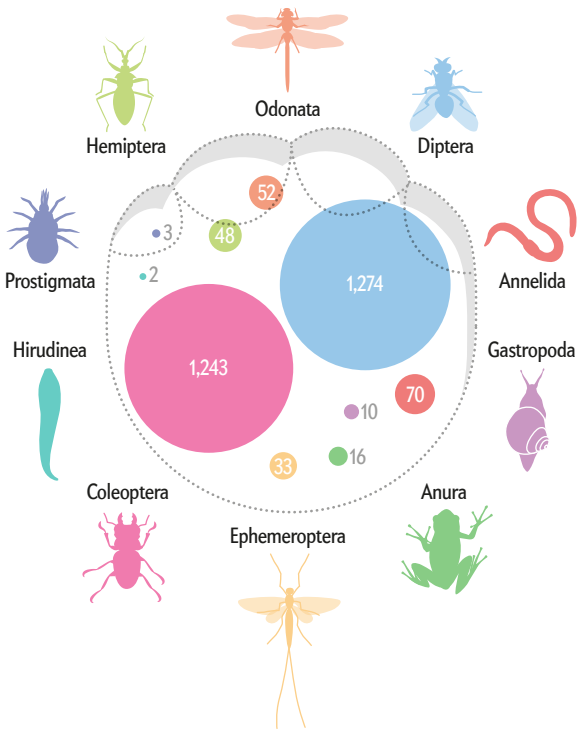
All told, the oldest footprints held the highest levels of biodiversity—probably because of a buildup of leaves and other organic detritus, which may serve as food. The study results were published online this past summer in the *African Journal of Ecology*.

The tally suggests that elephant footprints may have a place within the life cycles of several species and within the food web itself. "Who would have thought that something as innocuous as elephant footprints could be fundamental" to so many other species, says George Wittemyer, chair of the scientific board of Save the Elephants, who was not involved with the study.

The researchers acknowledge that this work is in its early stages and more needs to be done to understand how heavily the tiny denizens rely on these footprint worlds. Nevertheless, the study adds to a body of research showing elephants play vital roles in their ecosystems (such as seed dispersal via their large manure contributions), and lead author Wolfram Remmers of Koblenz-Landau says it serves as one more reminder of what we could lose if the poaching crisis in Africa continues. —*John R. Platt*

The Pool Party in a Pachyderm Print

Thousands of animals were found in 30 elephant footprints. Animals represented in the data below are grouped by order.



MORKEL ERASMUS *Getty Images (elephant)*; SOURCE: "ELEPHANT (*LOXODONTA AFRICANA*) FOOTPRINTS AS HABITAT FOR AQUATIC MACROINVERTEBRATE COMMUNITIES IN KIBALE NATIONAL PARK, SOUTHWEST UGANDA," BY W. REMMERS ET AL., IN *AFRICAN JOURNAL OF ECOLOGY*; PUBLISHED ONLINE AUGUST 23, 2016

Graphic by Amanda Montañez

KAYANA SZYMCZAK Redux Pictures

ENERGY

Winds of Change

The U.S. gets offshore wind

The first offshore wind farm in the U.S. is scheduled to begin operations this month off the coast of Rhode Island—a small but notable step forward, given that other offshore projects have run into stiff headwinds this side of the Atlantic. The five turbines that make up the Block Island Wind Farm will generate 30 megawatts of electricity—enough to power 17,000 homes on average.

It is a surprise (and frustration) to many that the facilities have not cropped up sooner, considering the potential that offshore wind has to reduce long-term dependence on fossil fuels—and to add new power options for coastal cities with limited real estate. In fact, offshore wind has taken off in Europe, producing a total of 11.5 gigawatts a year. Analysts put the U.S.'s potential at more than 2,000 gigawatts, which is almost double the current electricity use in this country. Yet efforts to launch offshore wind power have fallen short for myriad reasons. For one, electricity distributors have had little reason to pay the higher costs compared with cheaper onshore power sources, such as natural gas and hydroelectric plants. "There is a graveyard of U.S. offshore wind projects that have died after failing to secure a contract for the purchase of its electricity," says Alex Morgan, a wind energy analyst at Bloomberg New Energy Finance. It does not help that developers currently have to import expensive turbines from Europe or Asia because there is not a homegrown supply chain.

Similar financing challenges stalled Cape Wind, a project that envisioned 130 wind turbines off the coast of Cape Cod, Mass. That project also struggled against lawsuits by fishers, environmentalists and residents who did not want the structures to obstruct their view.

Deepwater Wind, the developer of the Block Island Wind Farm, minimized political opposition and financing costs by starting small, but it hopes to eventually build a 15-turbine, 90-megawatt offshore facility 30 miles southeast of Montauk on Long Island. Other efforts suggest that Block Island won't be alone for long. For instance, the state of Massachusetts recently signed an energy bill that requires the purchase of offshore wind power if facilities are built. That mandate, combined with existing offshore wind leases, could lead to 1.6 gigawatts of offshore wind power being produced by 2024, according to Bloomberg New Energy Finance. The Department of Energy has also dedicated an extra $40 million each for projects located near Maine and New Jersey and in Lake Erie.

If nothing else, the impending retirement of old coal, oil and nuclear power plants opens the door for offshore wind farms, says Jeff Grybowski, CEO of Deepwater Wind. But everything comes down to the competitiveness of this energy option in U.S. markets. "The chicken-and-egg game begins when a new market such as the U.S. will only build offshore wind if the price is not too high," Morgan says.

—Jeremy Hsu

POLICY

Science in the Elections

Scientific American rates the presidential candidates on 20 science questions

Many of the greatest challenges the U.S. faces in coming years—from climate change to the spread of antibiotic-resistant bacteria—require scientific expertise to develop workable solutions. For the past eight years, nonprofit organization ScienceDebate.org has spearheaded a grassroots effort to push presidential candidates to discuss these issues, which are every bit as important to America's future as international affairs or tax policy. This year the campaigns of the Democratic and Republican nominees have once again provided answers to 20 questions developed by leading scientific, engineering, health and other groups.

Four years ago *Scientific American* graded the answers given by Barack Obama and Mitt Romney on a 0-to-5 scale based on direct and complete answers; scientific accuracy; feasibility; sustainability; and potential benefits to health, education and the environment. We determined that the 2012 candidates were within striking distance of each other on most of their responses.

This year is a different story. Below are two questions, summaries of Hillary Clinton's and Donald Trump's answers, and our critiques. —*The Editors*

CLIMATE CHANGE

Earth's climate is changing, and political discussion has become divided over both the science and the best response. What are your views on climate change, and how would your administration act on those views?

CLINTON acknowledges that "climate change is an urgent threat and a defining challenge of our time." She then outlines a plan to "generate half of our electricity from clean sources," to cut "energy waste" by a third and to "reduce American oil consumption by a third" over the next 10 years. To achieve these goals, she plans to "implement and build on" current "pollution and efficiency standards and clean energy tax incentives." Clinton loses a point for not describing where she will find the money to pay for such initiatives. ★★★★☆

TRUMP refers to "climate change" with quotations marks, supposedly to signal that he still believes—as he has asserted in the past—that human-caused global warming is a hoax. He has vowed to withdraw from the Paris climate accord and suggests that "our limited financial resources" are best spent on clean water and antimalaria efforts—without acknowledging that the success of both also depends on how climate change is addressed. ☆☆☆☆☆

PUBLIC HEALTH

Public health efforts such as smoking cessation, drunk driving laws, vaccination and water fluoridation have improved health and productivity and saved millions of lives. How would you improve federal research and our public health system to better protect Americans from emerging diseases and other public health threats, such as antibiotic-resistant superbugs?

CLINTON argues that "we are not investing in public health preparedness and emergency response the way we should" and backs up her claim with evidence showing that spending on public health has "fallen more than 9 percent since 2008." She says she plans to tackle the problem in part by creating a "Public Health Rapid Response Fund" that offers "consistent, year-to-year budgets, to better enable" public health officials "to quickly and aggressively respond to major public health crises and pandemics." Clinton loses a point for not detailing how much money she thinks the rapid response budget should contain or how it will be funded. ★★★★☆

TRUMP suggests that "in a time of limited resources" public health spending may not provide "the greatest bang for the buck." In fact, studies show that public health efforts typically offer returns on investment of between 125 and 3,900 percent, depending on the program. Trump offers no indication that he has grappled with the issue in any detail. He also states that he will work with Congress to make sure that "adequate resources are assigned to achieve our goals"—not noting that Congress has still declined, as of press time, to approve money to deal with the Zika threat that has emerged in the southern U.S. ☆☆☆☆☆

Full responses to all 20 questions—including those from Green Party candidate Jill Stein and Libertarian Party candidate Gary Johnson—as well as our evaluation of them are available at www.ScientificAmerican.com/20-questions

JUSTIN SULLIVAN Getty Images (*Clinton*); DARREN HAUCK Getty Images (*Trump*)

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

The Problem with Tech Copycats

Phones and tablets work pretty much the same way no matter who makes them, and it's not good for consumers

By David Pogue

If you're a tech critic like me, you discover one thing about technology fans right away. They can be fairly militant in their allegiance to one tech company or another.

As you read readers' objections to a review you've written, you encounter one particular argument amazingly often: "[Name of disliked tech company] stole that idea from [name of preferred company]!"

Absolutely right. The borrowing of tech ideas has become almost absurdly predictable. Apple introduced Siri, the voice assistant, in 2011 (after buying the company that developed it). Google's copycat, Google Now, arrived a year later, and Microsoft's Cortana followed in 2014.

In the era of Steve Jobs, Apple was often the first to develop new product types. The iPod, for example, begat the Microsoft Zune. The iPhone spawned Google's Android phones. The iPad was the model for everyone else's look-alike tablets.

These days, though, Apple is equally likely to be the follower as the leader. Samsung's Galaxy Gear smartwatches debuted in 2013; the Apple Watch arrived two years later. Spotify reached the U.S. in 2011; the nearly identical Apple Music launched in 2015. Microsoft's Surface tablet arrived in 2012, with a screen cover that opened to reveal a flat keyboard. The iPad Pro, with similar features, followed in 2015.

It's not just product ideas. You can find the same cycle of mimicry in individual features. You could easily create a genealogy of, say, the right-click shortcut menu, or notifications that pop up in the upper-right corner of your screen, or precisely three autocomplete suggestions that appear above the keyboard on your phone.

At the dawn of tech culture, all of this might have seemed like an outrageous theft of intellectual property. It certainly did to Jobs, who famously directed his lawyers to sue Microsoft for duplicating the Mac's "look and feel" with Windows in 1988.

But Apple lost that lawsuit. The central premise of copyrights (for creative works) and patents (for inventions) is this: you can't protect an *idea*—only the execution of it. That, in the end, was the crux of the court's ruling in Microsoft's favor. (Never mind that the features Apple was proudest of—overlapping windows, commands in menus, and so on—were originally developed by Xerox and found their way into Apple's machines.)

For a while, copycats paid at least lip service to differentiation. In Windows Vista, Microsoft added a universal-search icon like the one on the Mac—but placed it at the lower left of the screen, not the upper right. It created little floating windows showing stock, weather, notes, and so on—but called them "gadgets" rather than "widgets," as Apple had.

Today, though, nobody even bothers. Amazon's popular Echo, introduced widely in 2015, takes the form of a cylinder that sits on a shelf and does an enormous range of tech tasks, from streaming music to answering questions in response to spoken commands, like a home version of Siri. This year Google revealed its own Google Home—which works so similarly, it could almost pass for a clone.

First problem: Apple, Microsoft, Samsung, Amazon and Google basically wind up with identical portfolios: similar phones, tablets, laptops, music services, e-mail services, payment systems, auto-dashboard software, etcetera. Bigger problem: This frenzy of idea stealing thwarts innovation. It's time-consuming and expensive to develop a new product. Copying, on the other hand, is cheap and easy. So why should a company bother to innovate? You don't reap much benefit from being first, except in the few months before the copycats come.

Pharmaceutical companies enjoy 20 years of patent protection before generic drugs are permitted; the idea is to let them recoup the billions they've put into developing new medicines. Maybe we should adopt a similar structure for tech products—with a period of exclusivity of something like 20 *months*.

That way we'd restore the incentive to keep inventing—and Mr. Jobs wouldn't be spinning quite so furiously in his grave. SA

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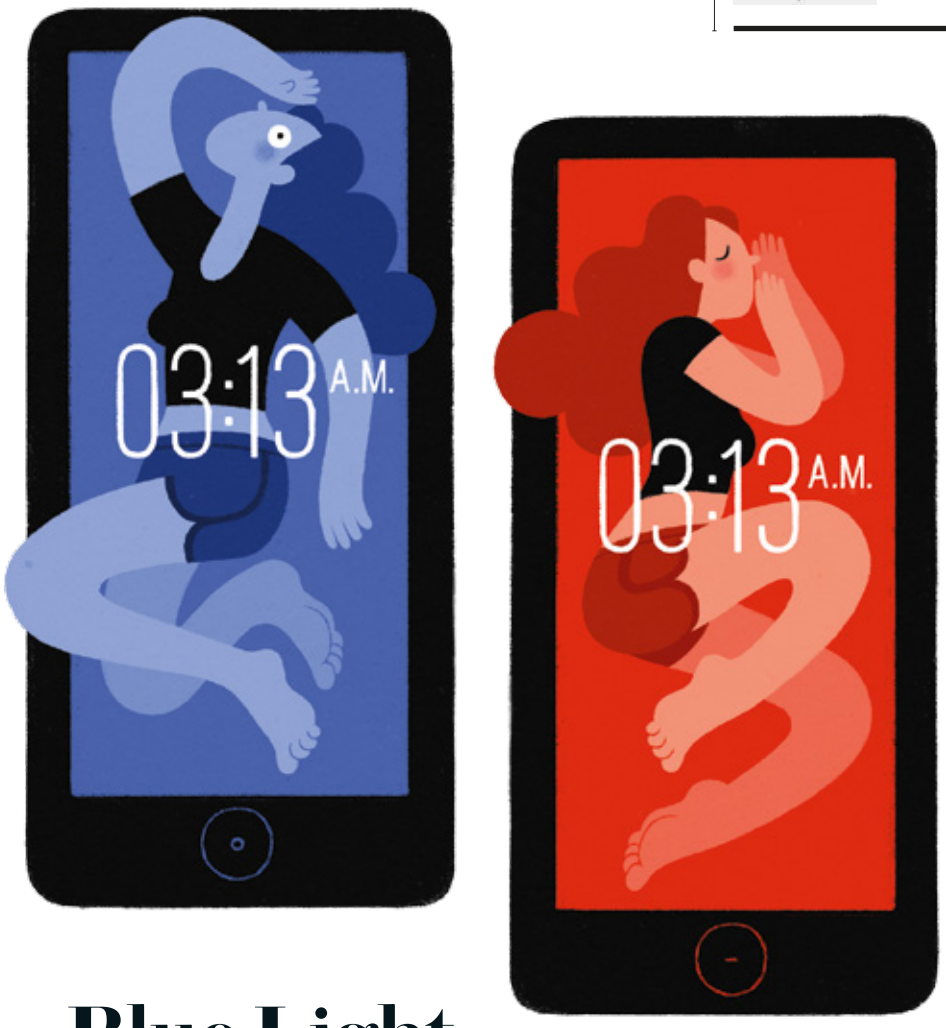
A SATIRICAL GUIDEBOOK TO WRITING TECH REVIEWS AND KEEPING READERS HAPPY: **SCIENTIFICAMERICAN.COM/NOV2016/POGUE**

Illustration by Jared Boggess

Ferris Jabr is a contributing writer at *Scientific American.*



Blue Light Blues

Why electronic screens keep you awake at night and what you can do about it

By Ferris Jabr

About a decade ago Los Angeles–based software developer Lorna Herf decided to try her hand at oil painting. She and her husband, Michael, also a computer programmer, eventually installed bright fluorescent lights in their apartment's loft so that Lorna could paint at night and still have an accurate sense of what colors on the canvas would look like during the day. Late one evening Lorna descended to the living room, where computer screens were aglow. Now that she had become more attuned to differences in lighting, she noticed just how much the bright light from the computer screens clashed with the soft warmth of the incandescent bulbs that surrounded them. She remembers thinking the electronic screens were "like little windows of artificial daylight," spoiling the otherwise gentle ambience of the room.

The tech-savvy couple engineered a crafty solution to minimize the discrepancy. They wrote some code to change the number and wavelength of the photons emitted by their computer screens as a day progressed. The Herfs' goal was to mimic natural shifts in ambient light as closely as possible, transitioning from the bright, bluish-white light characteristic of morning and afternoon sunshine to a dim, orange glow in the evening.

At first, they simply intended to harmonize the lighting scheme in their home. But they soon began to suspect that their new app, dubbed f.lux, might offer some health benefits as well. "After we'd been using it for a while, we started to notice it seemed easier to wind down at night," Lorna recalls, making it easier to fall asleep when they turned off their electronic devices. They are not the only ones who have appreciated the calming effect. Since the Herfs released the program for free in 2009, f.lux has been downloaded more than 20 million times.

By following their aesthetic taste, the Herfs had stumbled on a curious twist in the way the body controls how we sleep. Researchers have known for several decades that strong light of any kind can suppress melatonin, the hormone the brain produces at night to induce sleepiness. But more recent studies show that blue light suppresses melatonin more effectively than any other visible wavelength, potentially leaving people more alert when they would otherwise start feeling drowsy.

As it happens, smartphones, laptops and all kinds of electronic screens have become brighter and bluer over the past couple of decades because of the addition of powerful blue LEDs. During the day, when blue light is already naturally plentiful, a little extra exposure from electronic screens should not make much of a difference to anyone's physiology. The problem is that people are increasingly staring into bright screens long into the night.

Nearly everyone in a survey conducted by the National Sleep Foundation in 2011, for example, used a television, computer, cell phone or similar device within an hour of going to bed at least a few nights a week. In 2014 the same organization determined that 89 percent of adults and 75 percent of children in the U.S. have at least one electronic device in their bedroom, with a significant number of them sending or answering texts after

Illustration by Esther Aarts

they had initially fallen asleep. Motivated by such research, engineers and computer programmers are trying out various solutions to keep an already sleep-deprived population from losing more zzz's because of their electronic devices. The solutions range from tinted eyeglasses to naturalistic lighting systems for the home and office.

"If people can figure out ways to simulate changes in sunlight across the day, that would be perfect," says Christian Cajochen, head of the Center for Chronobiology at the University of Basel in Switzerland. "The ideal would be to have the same light throughout your home as outside of it." It remains to be seen how effective these remedies are, however, especially when compared with simply shutting the devices off.

TOO MUCH OF A GOOD THING

THE LIGHT EMANATING from electronic devices was not always such a hindrance to restful sleep. The current state of affairs can be traced to the 1992 invention in Japan of the high-brightness blue LED. By combining the new blue LEDs with older green and red ones or coating blue LEDs with chemicals that reemit other wavelengths, technology manufacturers could generate full-spectrum white LED light for the first time. Because LEDs are much more energy-efficient than their fluorescent predecessors, they soon became ubiquitous in TVs, computer screens, tablets and certain e-readers, infusing homes and offices with much brighter blue light than ever before.

Researchers did not begin amassing concrete evidence that blue LEDs can disrupt sleep until about 15 years ago, but they have had a good idea of the probable mechanism for quite some time. Scientists had discovered back in the 1970s that a tiny brain region dubbed the suprachiasmatic nucleus helps to control the body's sleep cycles, alertness, temperature and other daily fluctuations. Studies showed that the suprachiasmatic nucleus prompts the brain's pineal gland to produce melatonin every evening.

Earlier this century biologists uncovered exactly how this signaling process happens. As it turns out, the missing link was a previously unknown type of light-sensitive cell in the human eye, distinct from the familiar rods and cones that are responsible, respectively, for night and color vision. This third so-called photoreceptor tracks the amount of blue light in the environment and reports back to the suprachiasmatic nucleus. Thus, when there is a lot of blue light (as when the sun is overhead), this particular photoreceptor prompts the suprachiasmatic nucleus to tell the pineal gland not to make much melatonin, and so we stay awake. When the sun begins to set, however, the amount of blue light diminishes, triggering a surge in melatonin levels, prompting us to fall asleep.

Among the studies offering evidence that screens with blue LEDs might confuse the brain at night is a 2011 investigation by the University of Basel's Cajochen and his colleagues. In that work, volunteers exposed to an LED-backlit computer for five hours in the evening produced less melatonin, felt less tired, and performed better on tests of attention than those in front of a fluorescent-lit screen of the same size and brightness. Similarly, for subjects in a 2013 study led by Mariana Figueiro of the Rensselaer Polytechnic Institute, interacting with an iPad for just two hours in the evening was enough to prevent the typical nighttime rise of melatonin. And in a two-week trial at Brigham and Women's Hospital in Boston, published in 2014, volunteers who read on an iPad for four hours before bed reported feeling less sleepy, took an average of 10 minutes longer to fall asleep and slept less deeply compared with those who read paper books at night. Cajochen and others have also shown that these effects are especially pronounced in teens and adolescents, for reasons that remain unclear.

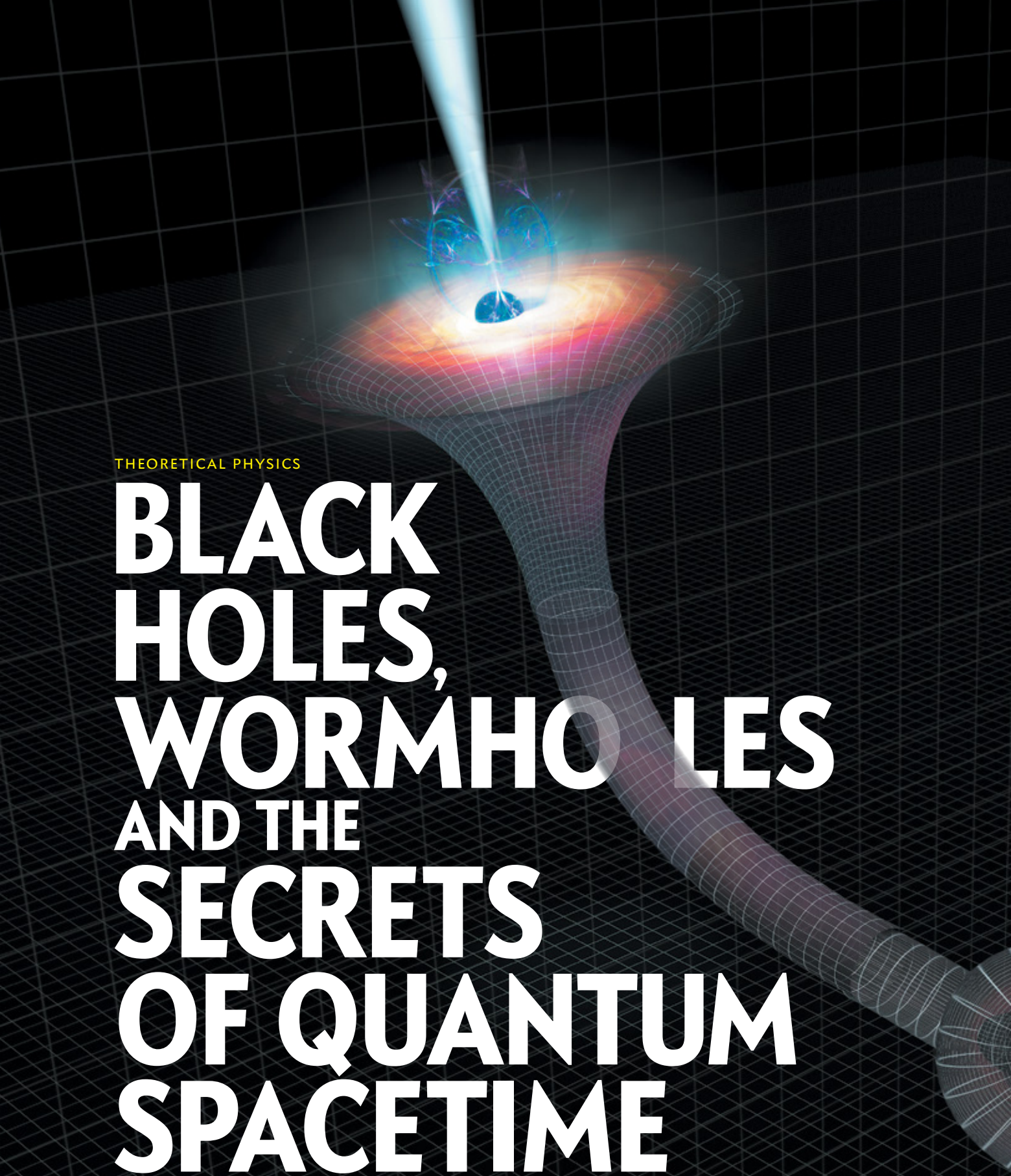
IN A NEW LIGHT

GIVEN THE ACCUMULATING EVIDENCE that artificial screens in general and blue lights in particular spoil sleep, scientists have begun investigating various remedies. Several studies have shown that wearing orange-tinted plastic goggles, which filter out the blue light emanating from electronic devices, helps to prevent melatonin suppression. Similar glasses are now commercially available for as little as $8 or as much as $100. A more expensive option is a so-called dynamic lighting system, which promises to re-create "the full range of natural daylight in an interior space" for hundreds to thousands of dollars depending on the size of one's home or office.

The most affordable countermeasures are computer programs such as f.lux. This past March, Apple introduced a function called Night Shift for the iPhone and iPad, which mimics f.lux in shifting the screen's emitted light "to the warm end of the spectrum" around sunset. So far no researchers have tested f.lux or Apple's Night Shift in a controlled study, but Figueiro says she is planning to conduct such experiments, and Michael Herf says he is collaborating with university scientists to examine the effects of f.lux in everyday environments outside the laboratory. "F.lux in my view is still a hypothesis," Herf adds. "We think it probably helps a lot of night owls, but we still need to support the anecdotes with data."

Researchers emphasize, however, that eliminating blue light is not a fail-safe solution. Even dim, orange screens make it tantalizingly easy to stay awake and read, watch movies or play games at night, keeping your brain alert when it should be winding down. "It's as if you're completely in the dark, but you drink coffee," Figueiro explains. "It's still going to have an effect."

Ultimately the surest solution is electronic abstinence: shutting off all screens and bright lights for at least a few hours before bedtime. The inescapable fact is that humans evolved to rise and sleep with the sun. "Before we had all this technology, before electricity and artificial lighting, we would be awake in daylight, have a little bit of fire in the evening, and then sleep," says Debra Skene, a chronobiologist at the University of Surrey in England. Artificial light has been enormously beneficial over the centuries. But there are times, especially at the end of the day, when it can be too much of a good thing. SA

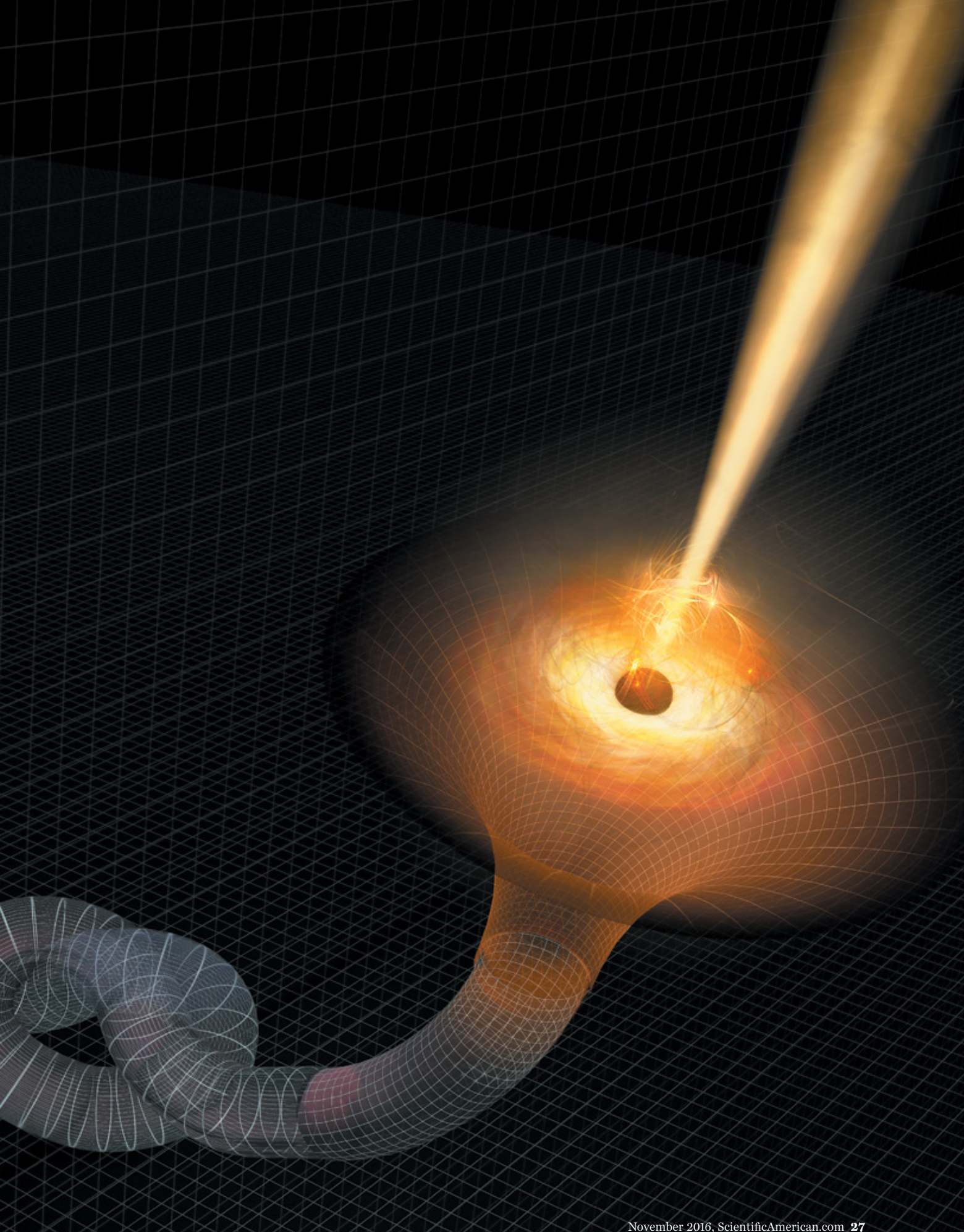


THEORETICAL PHYSICS

BLACK HOLES, WORMHOLES AND THE SECRETS OF QUANTUM SPACETIME

The weird quantum phenomenon of entanglement could produce shortcuts between distant black holes *By Juan Maldacena*

Illustration by Malcolm Godwin, Moonrunner Design



Juan Maldacena is a theoretical physicist at the Institute for Advanced Study in Princeton, N.J. He is known for his contributions to the study of quantum gravity and string theory. In 2012 he received a Breakthrough Prize in Fundamental Physics.

THEORETICAL PHYSICS IS FULL OF MIND-BOGGLING IDEAS, BUT TWO OF THE WEIRDEST ARE quantum entanglement and wormholes. The first, predicted by the theory of quantum mechanics, describes a surprising type of correlation between objects (typically atoms or subatomic particles) having no apparent physical link. Wormholes, predicted by the general theory of relativity, are shortcuts that connect distant regions of space and time. Work done in recent years by several theorists, including myself, has suggested a connection between these two seemingly dissimilar concepts. Based on calculations involving black holes, we realized that quantum mechanics' entanglement and general relativity's wormholes may actually be equivalent—the same phenomena described differently—and we believe the likeness applies to situations beyond black holes.

This equivalence could have profound consequences. It suggests that spacetime itself could emerge from the entanglement of more fundamental microscopic constituents of the universe. It also suggests that entangled objects—despite having long been viewed as having no physical connection to one another—may in fact be connected in ways that are far less fantastical than we thought.

Furthermore, the relation between entanglement and wormholes may help in developing a unified theory of quantum mechanics and spacetime—what physicists call a theory of quantum gravity—that derives the physics of the macroscopic cosmos from the laws that govern the interactions of the atomic and subatomic realms. Such a theory is necessary for understanding the big bang and the interior of black holes.

Interestingly, both quantum entanglement and wormholes date back to two articles written by Albert Einstein and his collaborators in 1935. On the surface, the papers seem to deal with very different phenomena, and Einstein probably never suspected that there could be a connection between them. In fact, entanglement was a property of quantum mechanics that greatly bothered the German physicist, who called it "spooky action at a distance." How ironic that it now may offer a bridge to extend his relativity theory to the quantum realm.

BLACK HOLES AND WORMHOLES

TO EXPLAIN WHY I think quantum entanglement and wormholes could be related, we must first describe several properties of black holes, which are intimately involved in this idea. Black holes are regions of curved spacetime that differ drastically from the relatively nondistorted space we are used to. The distinctive feature of a black hole is that we can separate its geometry into two regions: the exterior, where space is curved but objects and messages can still escape, and the interior, lying beyond the point of no return. The interior and exterior are separated by a surface called the event horizon. General relativity tells us that the horizon is just an imaginary surface; an astronaut crossing it would not feel anything special at that location. But having crossed it, a space traveler would be doomed to being squeezed into a region with huge curvature and with no possibility of escape. (In fact, the interior is actually in the future compared with the exterior, so the traveler cannot escape, because he or she cannot travel to the past.)

Just a year after Einstein introduced general relativity, German physicist Karl Schwarzschild found the simplest solution to Einstein's equations describing what would later be called black holes. The geometry that Schwarzschild came up with was so unexpected that it took until the 1960s for scientists to fully understand that it describes a wormhole joining two black holes. From the outside the black holes appear to be separate entities sitting at distant locations, yet they share an interior.

In a 1935 paper, Einstein and his colleague Nathan Rosen, then at the Institute for Advanced Study in Princeton, N.J., anticipated that this shared interior was a kind of wormhole (although they did not understand the full geometry it predicted), and for this reason wormholes are also called Einstein-Rosen (ER) bridges.

The wormhole in Schwarzschild's solution differs from black holes that form naturally in the cosmos in that it contains no

IN BRIEF

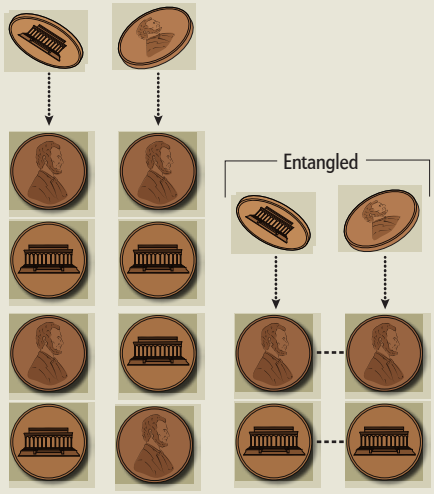
The laws of quantum physics allow for distant objects to be entangled so that actions on one affect the other, even though they lack a physical link.

The equations of relativity, which describe the geometry of spacetime, allow for wormholes: shortcuts between distant regions of space and time.

Physicists have suggested that the two phenomena might be equivalent and that this equivalence is a clue for developing a quantum description of spacetime.

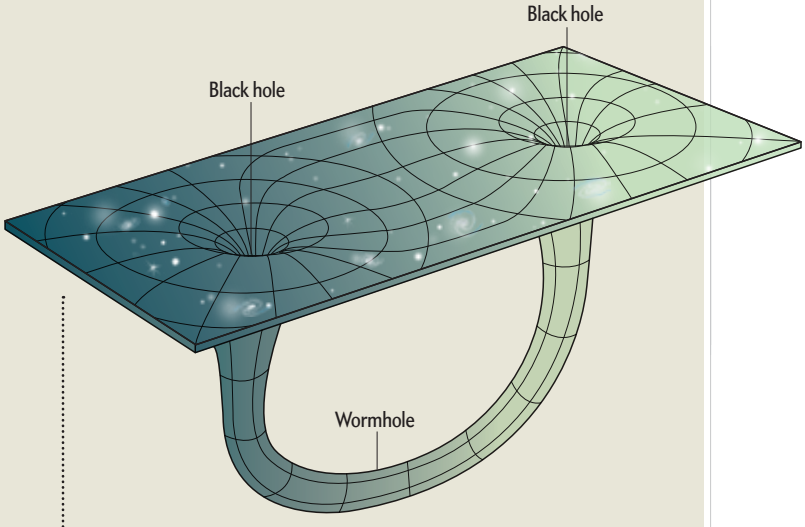
Entanglement Meets Wormholes

Entanglement is a concept from the theory of quantum mechanics describing a special type of correlation between two distant objects. Wormholes, which were predicted by general relativity, are theoretical bridges in spacetime joining distant black holes. Physicists now think that these two phenomena, seemingly disconnected, may be fundamentally related.



ENTANGLEMENT

When two normal coins are thrown, the outcome of one has no effect on the other—any two combinations might result. If two coins are entangled, however, then throwing the first coin determines what will happen to the second. If the first comes out heads, for instance, the second must be heads, and if the first is tails, so must the second be.

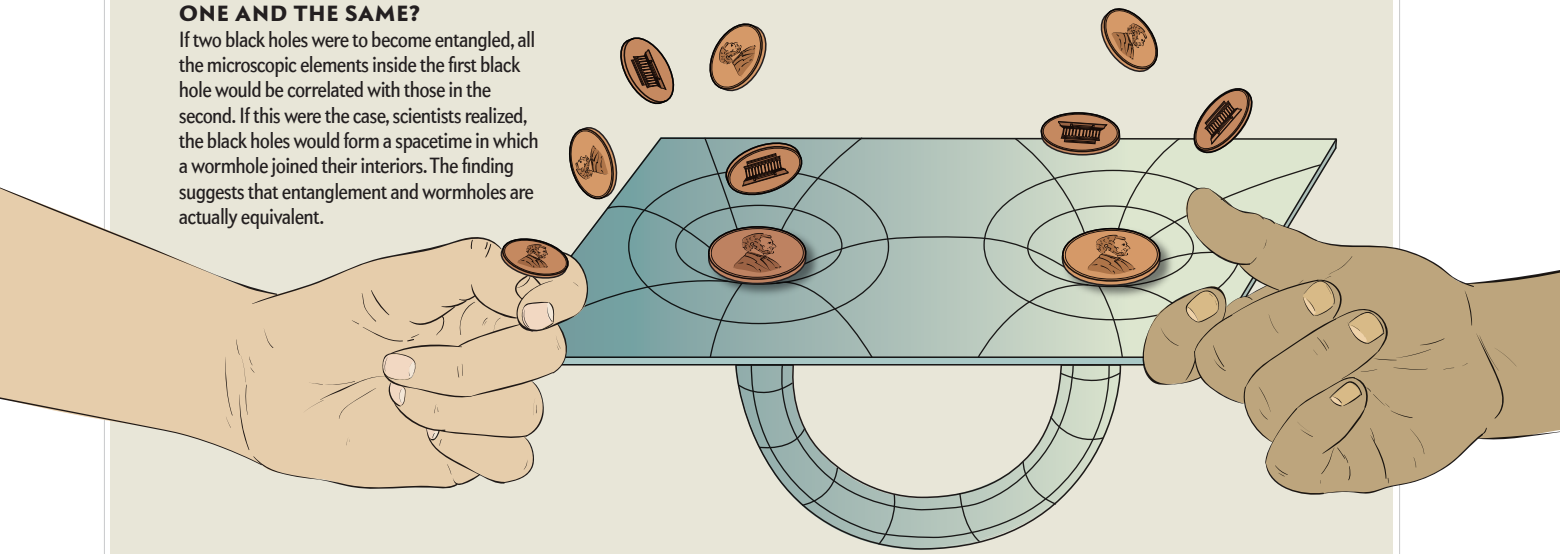


WORMHOLES

The equations of general relativity suggest that wormholes can connect two black holes, even those located vast distances apart, to create a bridge in spacetime. From the outside the two black holes would appear to be separate entities, but they would share an interior connecting them. No person or signal could travel through, however.

ONE AND THE SAME?

If two black holes were to become entangled, all the microscopic elements inside the first black hole would be correlated with those in the second. If this were the case, scientists realized, the black holes would form a spacetime in which a wormhole joined their interiors. The finding suggests that entanglement and wormholes are actually equivalent.



matter—merely curved spacetime. Because of the presence of matter, naturally formed black holes have only one exterior. Most researchers view the full Schwarzschild solution, with its two exteriors, as a mathematical curiosity irrelevant to the black holes in the universe. Nevertheless, it is an interesting solution and physicists have wondered about its physical interpretation.

The Schwarzschild solution tells us that the wormhole connecting the two black hole exteriors varies with time. It elongates and becomes thinner as time progresses, like stretching out a piece of elastic dough. Meanwhile the two black hole horizons, which at one point touch, separate rapidly. In fact, they pull apart so quickly that we cannot use such a wormhole to travel from one

Illustration by Jillian Ditner

exterior to the other. Alternatively, we can say that the bridge collapses before we can cross it. In the dough-stretching analogy, the collapse of the bridge corresponds to the dough becoming infinitesimally thin as it gets stretched more and more.

It is important to note that the wormholes we are discussing are consistent with the laws of general relativity, which do not allow faster than light travel. In that way they differ from science-fiction wormholes that allow instantaneous transport between distant regions of space, as in the movie *Interstellar*. Sci-fi versions often violate the known laws of physics.

A science-fiction story involving our type of wormhole might look like the following. Imagine two young lovers, Romeo and Juliet. Their families do not like each other and so put Romeo and Juliet on different galaxies, forbidding them to travel. These lovebirds are very smart, however, and manage to construct a wormhole. From the outside the wormhole looks like a pair of black holes, one in Romeo's galaxy and one in Juliet's galaxy. The lovers decide to jump into the interior of their respective black holes. Now, according to their families, they simply committed suicide by jumping in and are never heard from again. Unbeknownst to the outside world, though, the geometry of the wormhole is such that Romeo and Juliet actually meet in the shared interior! And they can live together happily for a while before the bridge collapses, destroying the interior and killing them both.

The traditional wisdom that nothing can escape a black hole is too simplistic.

QUANTUM ENTANGLEMENT

THE 1935 PAPER discussing the other phenomenon of interest to us—entanglement—was written by Einstein, Rosen and Boris Podolsky (also then at the Institute for Advanced Study). The three authors came to be known as EPR. In this famous work, the physicists argued that quantum mechanics allows for the existence of certain strange correlations between distant physical objects, a property that would only later be called entanglement.

Correlations between distant objects can also happen in classical physics. Imagine, for example, that you leave home with a single glove because you forgot the other one at home. Before searching your pocket, you do not know whether you have the left or right glove. Once you see that you have the right-hand glove, though, you will immediately know that the one at home is the lefty. But entanglement involves a different kind of correlation, one that exists between quantities governed by quantum mechanics, which are subject to Heisenberg's uncertainty principle. This principle says that there are pairs of physical variables that are impossible to know accurately at the same time. The best-known example involves the position and velocity of a particle: if we measure its position accurately, its velocity becomes uncertain, and vice versa. EPR wondered what would happen if we decided to measure either the positions or the velocities of the individual particles in a pair separated by a wide distance.

The example that EPR analyzed involves two particles with the same mass moving in a single dimension. Let us call these particles R and J because they are the particles that we will imagine being measured by Romeo and Juliet. We can prepare them in such a way that their center of mass has a well-defined position, which we will call x_{cm}, equal to x_R (the position of R) plus x_J (the position of J). We can require the center of mass to equal zero—in other words, we can say that the two particles are always equidistant from the origin. We can also make the particles' relative velocity, v_{rel}, equal to the velocity of R (v_R) minus the velocity of J (v_J), take a precise value; for example, v_{rel} equals some number we can call v_0. In other words, the difference between the two velocities must stay the same. We are here specifying a position and a velocity accurately but not for the same single object, so we do not violate Heisenberg's uncertainty principle. If we have two different particles, nothing prevents us from knowing the position of the first and the velocity of the second. Similarly, once we fix the position of the center of mass, we cannot say anything about the velocity of the center of mass, but we are free to fix the relative velocity.

Here we get to the most amazing part and the thing that makes quantum entanglement seem so strange. Suppose that our particles are far away from each other, and two distant observers, Romeo and Juliet, decide to measure the particles' positions. Now, because of how the particles have been prepared, if Juliet determines any specific value for x_J, then Romeo will find that his particle's position is the negative of Juliet's ($x_R = -x_J$). Note that Juliet's result is random: the position of her particle will vary from measurement to measurement. Romeo's result, however, is completely fixed by Juliet's. Now suppose they both measure their own particle's velocity. If Juliet gets a specific result for v_J, then Romeo will surely find that his velocity is the value of Juliet's plus the relative velocity ($v_R = v_J + v_0$). Again Romeo's result is completely determined by Juliet's. Of course, Romeo and Juliet are free to choose which variable they will measure. In particular, if Juliet measures the position and Romeo measures the velocity, their results will be random and will not display any correlation.

The strange thing is that even though Romeo's measurements of the position and velocity of his particle are constrained by Heisenberg's uncertainty principle, if Juliet decides to measure the position of her particle, Romeo's particle will have a completely certain position once he knows the result of Juliet's measurement. And the same thing will happen with the velocity. It appears as if, when Juliet measured the position, Romeo's particle immediately "knew" that it must have a well-defined position and an uncertain velocity, whereas the opposite should be the case if Juliet measured the velocity. At first glance this situation appears to allow an instantaneous transmission of information: Juliet can measure the position, and then Romeo would see a definite position for his particle, thus inferring that Juliet measured the position. Romeo would not be able to realize, however, that his particle has a definite position without knowing the actual value of the position that Juliet measured. So in fact, correlations caused by quantum entanglement cannot be used to send signals faster than the speed of light.

Although it has been experimentally confirmed, entanglement may still seem just an esoteric property of quantum systems. Yet during the past two decades these quantum correlations have led

SCIENTIFIC AMERICAN ONLINE Watch a video about quantum entanglement at ScientificAmerican.com/nov2016/entanglement

to a number of practical applications and breakthroughs in fields such as cryptography and quantum computing.

EQUIVALENCE

HOW MIGHT OUR TWO very different, bizarre phenomena—wormholes and entanglement—be related? A further look at black holes points the way to the answer. In 1974 Stephen Hawking showed that quantum effects will cause black holes to emit radiation in the same way a hot object does—proving that the traditional wisdom that nothing can escape a black hole is too simplistic. The fact that black holes radiate implies that they have a temperature—a notion with important ramifications.

Since the 19th century physicists have known that temperature stems from the movement of the microscopic constituents of a system. In a gas, for example, temperature arises from the agitation of molecules. Therefore, if black holes have temperatures, one can expect that they also have some kind of microscopic constituents that collectively are capable of adopting various possible configurations, or so-called microstates. We also believe that, at least as seen from the outside, black holes should behave as quantum systems; that is, they should be subject to all the laws of quantum mechanics. In summary, when we look at a black hole from the exterior we should find a system that can have many microstates, with the probability of its being in any of these configurations essentially equal for each microstate.

Because black holes look like ordinary quantum systems from the outside, nothing prevents us from considering an entangled pair of them. Imagine a couple of very distant black holes. Each has a large number of possible microscopic quantum states. Now imagine an entangled pair of black holes in which each quantum state in the first black hole is correlated with the corresponding quantum state of the second. In particular, if we measure a certain state for the first hole, the other hole must be in exactly the same state.

The interesting thing is that, based on certain considerations inspired by string theory (one approach toward a theory of quantum gravity), we can argue that a pair of black holes with their microstates entangled in this way (that is, in what might be called an EPR entangled state) would produce a spacetime in which a wormhole (an ER bridge) links the interior of both black holes. In other words, quantum entanglement creates a geometric connection between the two black holes. This result is surprising because entanglement, we thought, involves correlations without a physical connection. But the two distant black holes in this case are physically connected through their interior and brought close via the wormhole.

Leonard Susskind of Stanford University and I have called the equivalence of wormholes and entanglement "ER = EPR," because it relates the two articles that Einstein and his colleagues wrote in 1935. From EPR's point of view, the observations near the horizons of each black hole are correlated because the black holes are in a state of quantum entanglement. From ER's vantage point, the observations are correlated because the two systems are linked through the wormhole.

Now, going back to our Romeo and Juliet sci-fi story, we can see what the lovers should do to form an entangled pair of black holes to produce the wormhole. First they need to create many entangled particle pairs, similar to the ones discussed earlier, with Romeo possessing one member of each entangled pair and Juliet the other. They then need to build very complex quantum computers that will manipulate their respective quantum particles and combine them in a controlled way to create a pair of entangled black holes. Such a feat would be terribly hard to achieve in practice, but it seems possible according to the laws of physics. Besides, we did say Romeo and Juliet were very smart!

A UNIVERSAL PRINCIPLE?

THE IDEAS THAT LED US HERE have been developed over the years by many researchers, beginning with a 1976 article by Werner Israel, then at the University of Alberta. There was also interesting work in 2006 on the connection between entanglement and the geometry of spacetime by Shinsei Ryu and Tadashi Takayanagi, both then at the University of California, Santa Barbara. Susskind and I were motivated by research published in 2012 by Ahmed Almheiri, Donald Marolf, Joseph Polchinski and James Sully, all then at U.C. Santa Barbara. They discovered a paradox related to the nature of an entangled black hole's interior. The ER = EPR idea, which says that the interior is part of a wormhole connecting the black hole to another system, alleviates some aspects of this paradox.

Although we identified the connection between wormholes and entangled states using black holes, it is tempting to speculate that the link is more general—that whenever we have entanglement we have a kind of geometric connection. This expectation should hold true even in the simplest case, in which we have only two entangled particles. In such situations, however, the spatial connection could involve tiny quantum structures that would not follow our usual notion of geometry. We still do not know how to describe these microscopic geometries, but the entanglement of these structures might somehow give rise to spacetime itself. It is as if entanglement can be viewed as a thread connecting two systems. When the amount of entanglement becomes larger, we have lots of threads, and these threads could weave together to form the fabric of spacetime. In this picture, Einstein's relativity equations are governing the connections and reconnections of these threads; quantum mechanics is not just an add-on to gravity—it is the essence of the construction of spacetime.

For now, this picture is still wild speculation, but several clues point toward it, and many of us physicists are pursuing its implications. We believe that the seemingly unrelated phenomena of entanglement and wormholes might in fact be equivalent and that this equivalence provides an important clue for developing a description of quantum spacetime—and a long-awaited unification of general relativity and quantum mechanics. SA

MORE TO EXPLORE

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scientificamerican.com/magazine/sa

HUMAN ORGANS FROM ANIMAL BODIES

Juan Carlos Izpisúa Belmonte is a professor at the Gene Expression Laboratory at the Salk Institute for Biological Studies.

BIOLOGY

Scientists are taking the first steps toward growing replacement parts for people inside pigs, cows and other animals

By Juan Carlos Izpisúa Belmonte

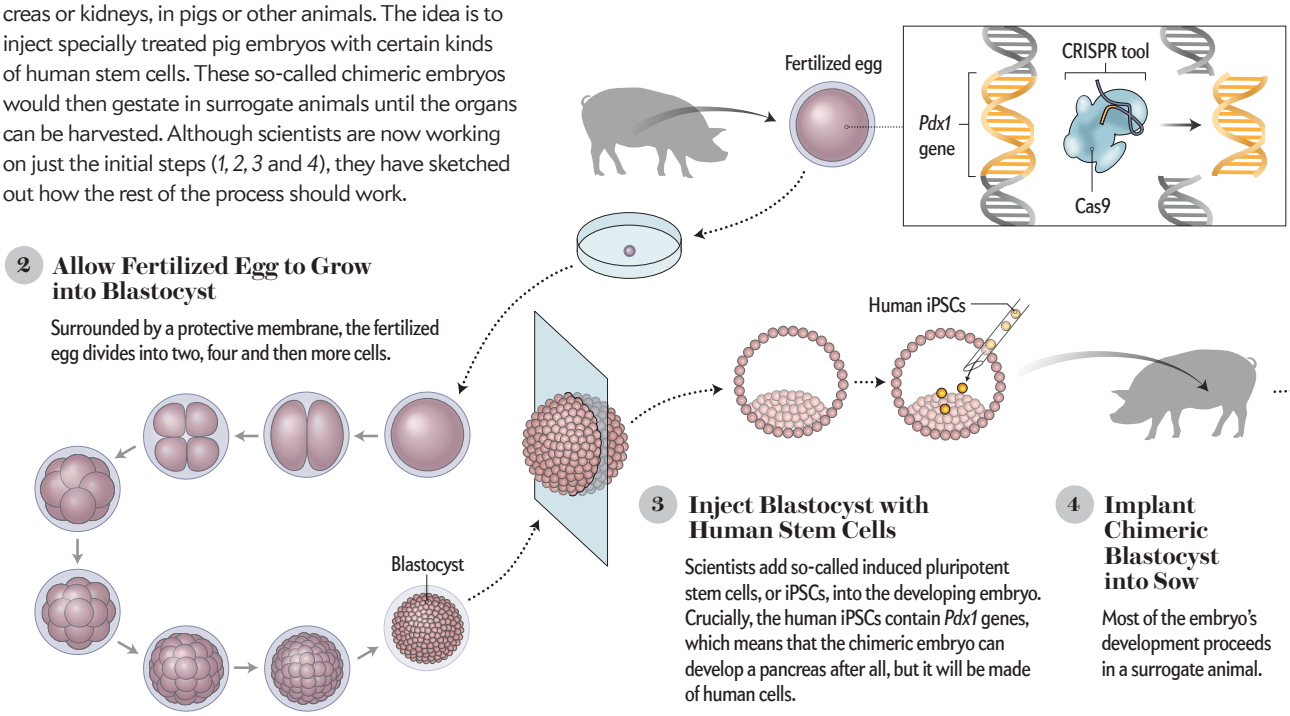
TENS OF THOUSANDS OF people around the world receive organ transplants every year. Although the medical know-how for transplanting organs has expanded rapidly, the number of donated organs has lagged. Global figures are hard to come by, but an average of 16 people in Europe and 22 in the U.S. die every day while waiting for a replacement heart, liver or other organ. Moreover, the gap between the number of people who need a new organ and the number of organs available for donation keeps widening.

One way to alleviate the shortage would be to grow replacement organs in the laboratory. A few years ago scientists thought that they could do that by using stem cells, which are progenitor cells that can give rise to different kinds of tissues, and an artificial scaffold to create a new organ. Investigators have struggled, however, to orchestrate the development of stems cells to produce a fully functioning human organ. Research continues on this approach, but progress has been slow.

Illustration by Peter Horvath

The Research Plan

Recent advances in stem cell technology may one day allow researchers to grow human organs, such as a pancreas or kidneys, in pigs or other animals. The idea is to inject specially treated pig embryos with certain kinds of human stem cells. These so-called chimeric embryos would then gestate in surrogate animals until the organs can be harvested. Although scientists are now working on just the initial steps (*1*, *2*, *3* and *4*), they have sketched out how the rest of the process should work.



A small but increasing number of investigators, myself included, think that there may be another way: let nature do the heavy lifting. Evolution has already created an exquisite process for turning a handful of identical cells into all the specialized organs and tissues needed to build an entire complex organism—whether it is a mouse or a person. That virtuoso performance occurs in the weeks and months after a fertilized egg gives rise to an embryo that grows and—without having to rely on an artificial scaffold—develops into a full-grown animal with a well-formed heart and lungs, kidneys and other tissues. We believe we can figure out a way to harvest organs from animals, such as pigs, for use in people.

A normal pig heart would, of course, be of little use to a human in need of a transplant. For starters, our immune systems would overwhelmingly reject a direct cross-species implant. (Pig heart valves are suitable substitutes for human tissue only after they have been chemically treated to prevent this immune reaction—a process that would destroy a complex organ's ability to function.) My colleagues and I believe that it may be possible to grow human organs—made entirely, or almost entirely, of human cells—in an animal such as a pig or cow. The resulting animal would be a chimera—a creature that combines the parts of two different species, much like the mythical griffin, which sports the head and wings of an eagle and the body of a lion. Our dream is to create a chimera by injecting human stem cells into carefully prepared animal embryos so that when they become fully grown, they contain some organs made up of human cells. After sacrificing the animal, we would then harvest the single heart, liver or kidney made up of human cells and give it to a person in need of a transplant.

The idea might sound far-fetched, but researchers in the U.S. and Japan have already shown that it is possible in principle. Several different teams injected custom-designed mouse embryos with rat stem cells and then allowed the resulting chimeras to develop in surrogate mouse mothers. After a few weeks of gestation, the surrogates gave birth to animals that looked and acted like

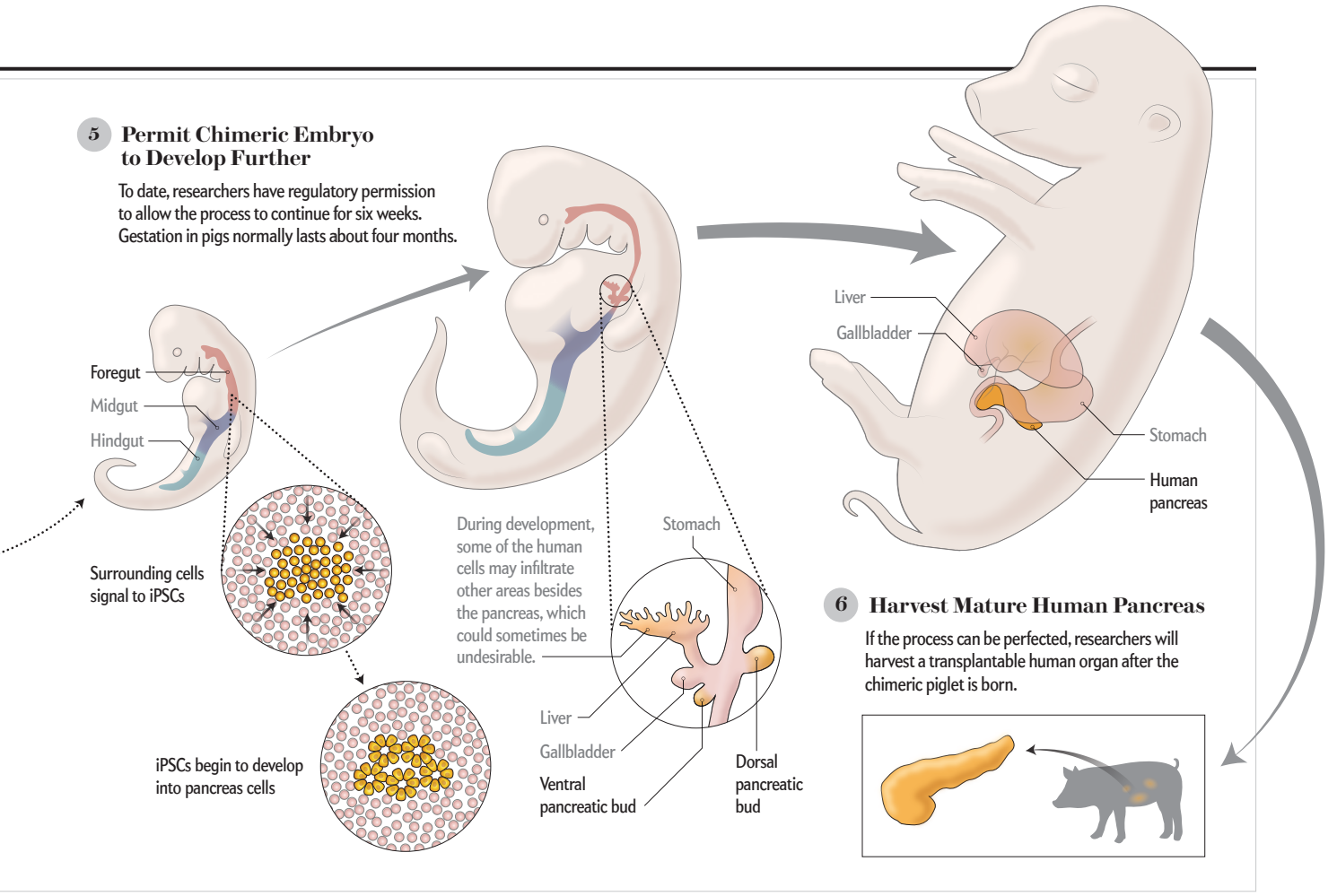
IN BRIEF

Biologists are trying to figure out how to grow human organs inside of animals, such as pigs, using the latest advances in stem cell technology. Such an achievement could dramatically decrease current organ-transplant shortages.

The idea is to take human stem cells and implant them, under the right conditions, into specially prepared pig embryos so that the resulting organism, known as a chimera, develops into an animal with a human pancreas, kidney or other organs.

If early experiments are successful and investigators obtain the necessary regulatory permissions from local and national authorities, the goal is to allow the chimeras to develop full-term (about four months for pigs) to see if they produce usable human organs.

Graphic by Amanda Montañez



mice—except that they had the pancreas of a rat. Researchers in my lab and in other groups have taken the next step and injected human stem cells into porcine embryos. A few of these injections "took," and we confirmed that the human tissue had started to mature normally. Then we transferred the chimeric embryos into surrogate sows, where we have allowed them to develop for three to four weeks. After completing several more intermediate experiments, we will permit the embryos to grow a couple of months, at which point we will determine how many of their cells are of human origin. Provided these experiments are successful—and we receive permission from state and local authorities to continue—we expect to enable the embryos to grow full-term (which for pigs is about four months).

We are nowhere near ready to take that final step of producing chimeric piglets. We still have much to learn about how best to prepare human stem cells and animal embryos so that the chimeras will remain viable throughout pregnancy. A lot could go wrong. But even if we are unable to create fully formed organs, the techniques we discover should help us better understand the onset, progression and clinical outcome of many complex and devastating illnesses, including cancer. If successful, this approach could have enormous implications for organ-transplant therapies. Waiting lists could become a thing of the past as we develop a bountiful supply of replacement parts from farm animals for tens of thousands of suffering people around the world.

LEARNING FROM NATURE

IN RECENT YEARS biologists have learned so much about how embryos grow that we have tentatively begun to tailor the process to our bidding. We also recognize how much this growth is guided by the precise location of different cells at various times within the developing organism. The cells make and release specialized proteins called growth factors that, depending on their concentration within distinct regions of the embryo, in turn activate and silence a raft of internal genetic programs. Relying on this still incomplete understanding and a lot of trial and error, researchers in our lab and elsewhere are manipulating pig embryos so that they produce tissues that would eventually give rise to a human kidney, pancreas or other organ.

The raw materials we use include porcine eggs and sperm (taken from animals) and human stem cells (grown in cell cultures). We fertilize a pig egg with pig sperm, and a few hours later the combined cell, now known as a zygote, divides into two and then four seemingly identical cells. Each of these cells activates the same groups of genes in its DNA, which leads to the production of various proteins that coax the cells, among other things, to divide even further.

Thanks to the complex interplay of genes and proteins, these once identical cells soon start to move and behave differently as they divide. Within a few days several hundred cells have formed a kind of ball within a ball, known as the blastocyst. This is the latest point at which we can inject the human stem cells—

before the specialized tissues, known as primordia, that will later give rise to functioning organs start to form. If we wait any longer, the rest of the stem cells in the host embryo will simply ignore the foreign stem cells, which will then shrivel up and die.

As the embryo grows, it forms outer, middle and inner layers, and any individual cell's precise location within the larger whole becomes more important than ever before. Previous work has demonstrated, for example, that certain cells within the inner layer of the embryo respond to the protein signals in their microenvironment by turning on the gene *Pdx1*. This step in turn activates many other genes that trigger the maturation of the pancreas. A few cells located in the middle layer, in contrast, react to external signals by turning on the gene *Six2,* which starts the formation of the kidneys. Thus, although all cells in the body contain the same DNA sequences, the particular environment in which a cell finds itself during a specific stage of development determines which genes are turned on or off and thus what kind of tissue it will become.

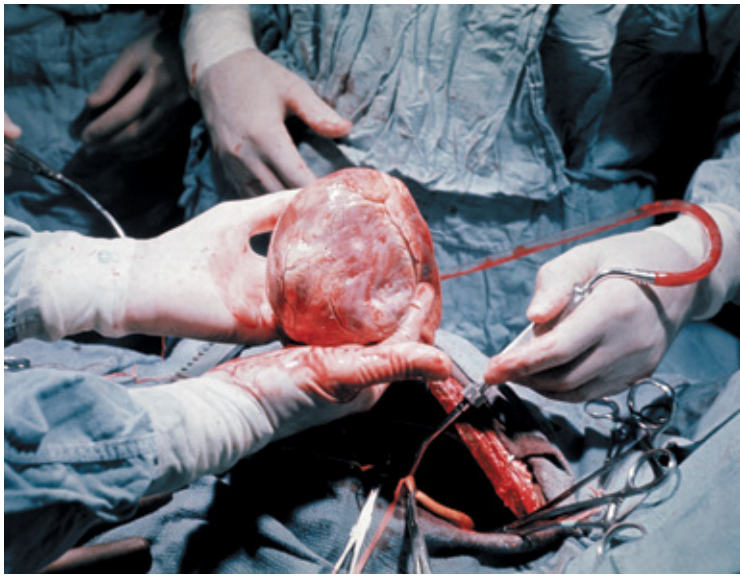
The fact that a single gene, such as *Pdx1* or *Six2,* can turn on an entire pathway leading to the formation of a pancreas or kidney turns out to be very important in our quest. By deleting the one critical gene needed for growing a pancreas (a process that my colleagues and I call "emptying the niche"), our lab has created pig embryos that will not grow the insulin-producing organ unless we inject enough human stem cells that contain the missing gene. If the added cells develop appropriately, they will give rise to a mature organ made entirely of human cells. The rest of the animal will, ideally, be made up of pig cells.

As with so many things in science, figuring out exactly how to empty an embryonic niche and then fill it with stem cells from a different species first took a lot of experiments on rodents. Finally, in 2010, Hiromitsu Nakauchi, then at the University of Tokyo, and his colleagues reported that they had successfully grown a mouse with a rat pancreas. More recently, my lab has been able to genetically reprogram mouse embryos so that they will use stem cells from rats to grow cells in their eyes. After three weeks of gestation in surrogate mouse mothers, these embryos become fetal mice with rat cells in their eyes.

CHALLENGES

EACH STEP ON OUR JOURNEY requires careful consideration of different potential problems. Because mice are too small to generate organs that would be a useful size for human patients, we have now concentrated our efforts on creating pig embryos. Pigs, and their organs, can grow to almost any proportion that transplant surgeons might need to help people of varying builds. Pigs also have a longer gestation period than mice do (about 20 days for the latter). Because normal human embryos require nine months to develop fully, researchers are inventing certain biochemical tricks to help human stem cells speed up their internal clocks so that they mature, or differentiate, on the host embryo's schedule. Adapting human cells to the somewhat longer pig timeline should require less effort than aligning with the much shorter mouse timeline.

Currently my colleagues and I have focused on growing a pancreas or kidney made of human cells because we know that a single gene kicks off its development in the embryo—a fairly straightforward process. Other organs, such as the heart, however, may depend on several genes to initiate the process, which means that emptying the niche for these organs will require deleting more than one gene, which is much more difficult. Recently researchers led by George Church of Harvard University have adapted the CRISPR/Cas9 gene-editing tool so that they can remove several genes from different locations in an embryo's DNA. Thus, investigators are prepared if it turns out that we need to do more sophisticated genetic manipulation to create other organs.



HUMAN DONORS: Patient survival has improved since this heart was transplanted in 1968, but organ shortages have grown.

A bigger problem has been making sure that the human stem cells that are used are pristine enough to give rise to any kind of tissue. Biologists refer to this physiological state as being "developmentally naive." Human embryonic stem cells, which could be harvested from the leftover zygotes generated by in vitro fertilization clinics, would fit the bill, but their use would prove highly controversial.

Over the past decade researchers made a number of technical advances that looked, at first glance, as though they might solve the dilemma. They figured out how to coax mature cells taken from the skin or gut of an adult into becoming a kind of stem cell called an induced pluripotent stem cell, or iPSC. Experimenting on human iPSCs instead of human embryonic stem cells would certainly be more ethically acceptable. Using iPSCs would offer the added advantage of one day allowing scientists to create organs that are a genetic and immunological match for individual patients.

Closer study of the human iPSCs created to date, however, shows that they are not as naive as they need to be to survive inside a chimeric embryo. They are already so far along to becoming one of several specific cell types that they can no longer react to any of the biochemical signals coming from the embryo that tell them to grow into something else. Because these iPSCs do not respond correctly, the developing embryo ejects them as foreign.

Recently Jun Wu in my lab has begun treating human iPSCs with a unique combination of growth factors that allow a few of them, at least, to react appropriately to a wider range of embryonic signals. To date, our group has obtained preliminary results showing that our treated human iPSCs can, in fact, integrate into blastocysts. My colleagues and I stopped the experimental embryos from growing at different times after fertilization and ana-

GETTY IMAGES

SCIENTIFIC AMERICAN ONLINE Watch Izpisúa Belmonte talk about developmental biology at ScientificAmerican/nov2016/dev-bio

lyzed them under the microscope to check how well the host and donor cells had mixed. Next, we plan to allow the embryos to develop a little longer—until they are six weeks old, and the primordia can be seen. At that point, the embryos will begin generating the precursors of the body's various tissues and organs.

Even if we are able to produce human iPSCs that can fully integrate into pig embryos, however, we are not home free. Humans and pigs are not as closely related, evolutionarily speaking, as the mice and rats that have already been used to create chimeric animals. Thus, human iPSCs simply may have lost the ability to perceive all the biochemical signals from a more distantly related species such as pigs. If we cannot figure out a biochemical work-around to this problem, we may need to start testing our ideas in other species, such as cows.

NEXT STEPS

IN 2012 I DISCUSSED THESE and other concerns with my collaborator Josep Maria Campistol, general director of the Hospital Clinic of Barcelona, which is internationally known for its organ-transplantation services. I vividly remember his advice: "The only way to determine whether human iPSCs can cross species barriers and contribute to the formation of a human organ in a pig is to role up your sleeves and do the experiment," he said.

Campistol's pronouncement jolted me into action. I knew our lab would not be able to accomplish such a task by ourselves. Together with embryologists, veterinarians, stem cell biologists and bioethicists, my colleagues and I created an international consortium to test our ideas. We began injecting pig embryos with human iPSCs in 2015. I am especially grateful to the San Antonio Catholic University of Murcia in Spain and the Moxie Foundation for supporting this early work when no one thought our approach was even feasible.

To date, most of our experiments have been conducted in California and Spain—under the supervision of local and national regulatory agencies. So far we have allowed the chimeric pig-human embryos to gestate in a sow for about four weeks—at which point we sacrifice the animals. (The guidelines that we have worked out with regulatory authorities require us to sacrifice both surrogates and embryos.)

Overall, the results obtained from these and other experiments have helped us to gain some basic knowledge about the development of chimeric embryos. We are starting to learn the best number of human iPSCs that need to be implanted for the embryo to develop successfully and the time at which we need to implant them. We have also begun tracing the way the human cells start to migrate to different parts of the embryo.

AN ETHICAL BALANCE

EVEN AS WE SCIENTISTS perfect our procedures, however, we must work with the larger public to address the new ethical, social and regulatory challenges created by this emerging field. Our consortium worked closely with ethicists and regulators in California and Spain for a year and a half to develop the guidelines that govern our research.

It goes without saying that we abide by the standard rules regarding animal welfare that should apply to all research with sentient creatures—to avoid unnecessary pain and to provide adequate living space and exercise, among other things. There are additional concerns, however, that are specific to this technology. Truly naive stem cells, as I have said, can give rise to any kind of tissue. But we must pay special attention to three types—nerves, sperm and eggs—because humanizing these tissues in animals could give rise to creatures that no one wants to create.

Imagine the ethical nightmare, for example, if enough human nerves populated a pig's brain that it became capable of higher-level reasoning. We can forestall that problem by deleting the genetic program for neural development from all human iPSCs before we inject them. Then, even if human stem cells managed to migrate to the embryonic niche responsible for growing the brain, they would be unable to develop further. The only neurons that could grow would be 100 percent pig.

Another scenario researchers want to avoid, for reasons that will soon become clear, is the breeding of chimeric animals with each other. Although it is a long shot, there is always the chance that some of the human stem cells we implant could migrate to the niche that gives rise to the reproductive system instead of staying in the one that yields the desired organ. The result would be animals that produce sperm or eggs that are virtually identical to those found in people. Allowing these animals to then breed could lead to the ethically disastrous case in which a fully human fetus (the result of a humanized sperm from one pig fertilizing a humanized egg from another) starts growing inside a farm animal. The best way to prevent such a troubling outcome is to make sure that each chimeric animal used for transplantation is created from scratch, so to speak, by fertilizing eggs from a pig with sperm from a pig and then adding the human stem cells.

All bets are off, of course, if the technical challenges prove insurmountable. Yet even if we fail to create functional organs for transplantation, I believe the knowledge and techniques we discover along the way will prove enormously valuable. One of the first fields to benefit will most likely be cancer research. Studies show that many tumors grow uncontrollably in a child or adult by reactivating some (but not all) of the genes that once allowed the embryo to grow into a fetus. Thus, the better investigators understand the normal cellular signals that allow embryos to grow—and tell them when to stop growing—the better they may be able to coax cancer cells into abandoning their treacherous path.

Scientists are people, too, of course. We get excited about new ideas and novel ways of doing things. And we can be overly optimistic about what our discoveries may imply—not just for our own fields but also for humankind. But the preliminary results I have described in this article make me cautiously optimistic that we may generate human organs from chimeric animal embryos in the next couple of decades. SA

MORE TO EXPLORE

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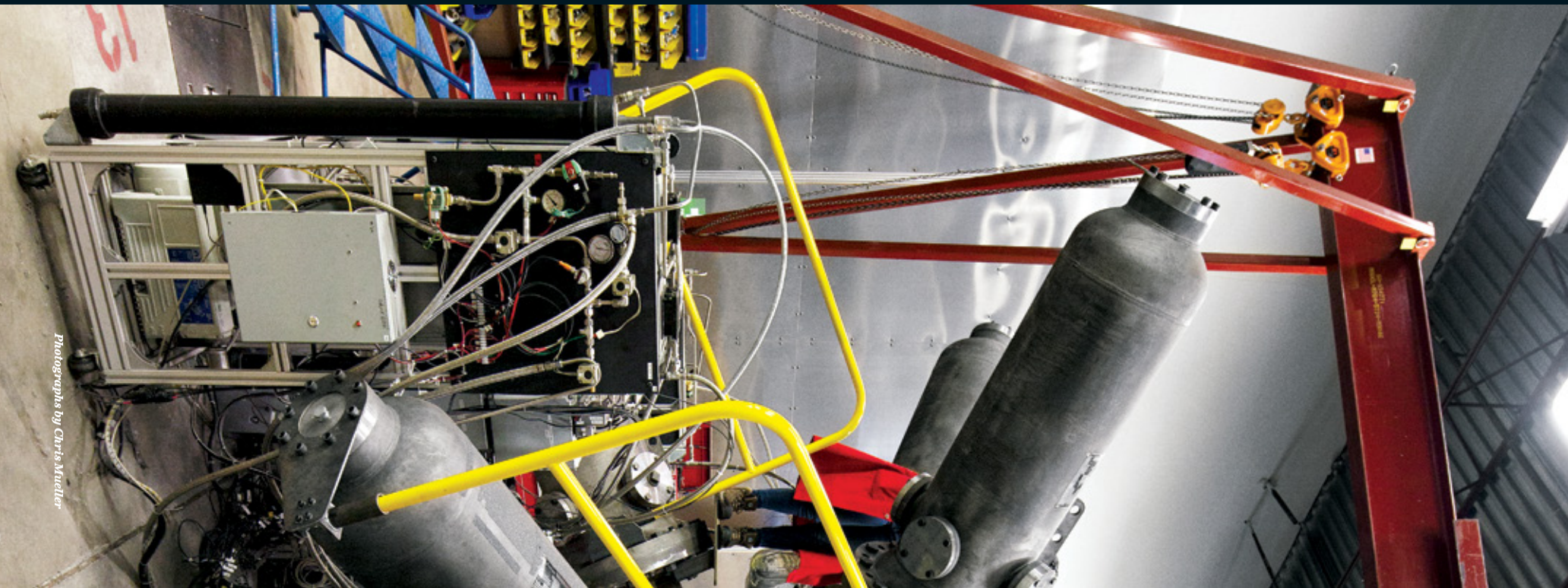
scientificamerican.com/magazine/sa

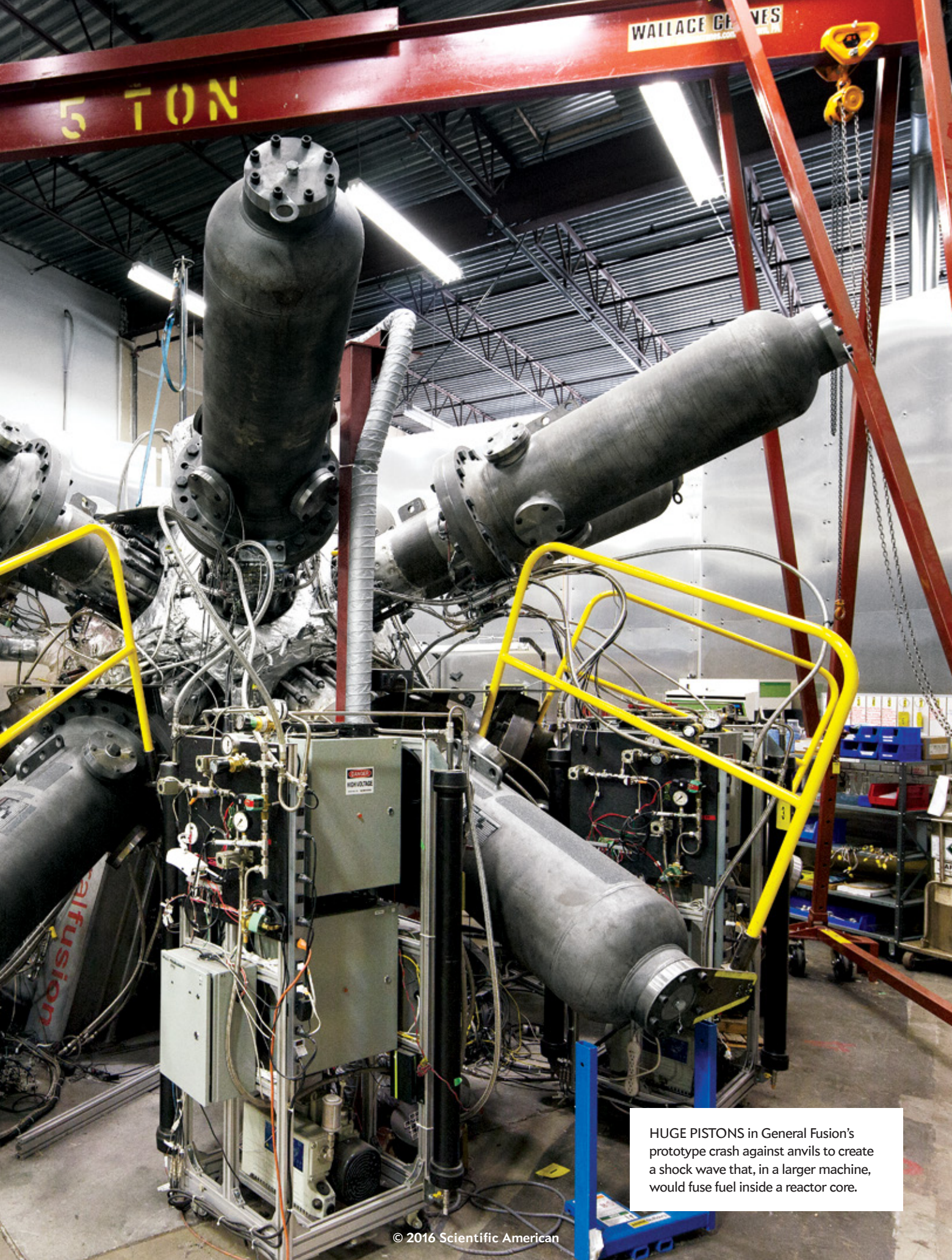
ENERGY

THE FUSION UNDERGROUND

A few bold physicists—some backed by billionaires—are exploring faster, cheaper roads to the ultimate source of clean energy *By W. Wayt Gibbs*



Photographs by Chris Mueller



HUGE PISTONS in General Fusion's prototype crash against anvils to create a shock wave that, in a larger machine, would fuse fuel inside a reactor core.

Sitting in the control room

of Tri Alpha Energy's experimental fusion reactor, in front of computer screens labeled "plasma guns" and "shot control," I feel slightly anxious as we make preparations to fire. This reactor is an early prototype for a power plant that would generate energy in a controlled version of what happens inside stars and H-bombs.

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On the video feed overhead, I see workers out on the floor of this nondescript warehouse near Irvine, Calif., walking away from the large reactor toward the doors. The shiny, cylindrical vacuum chamber at the reactor's center, about as long as two school buses parked bumper to bumper, is encircled by two dozen ring-shaped electromagnets, each taller than I am and as thick as my leg. The temperature inside that chamber will rise, on my command, to around 10 million degrees Celsius—though only for an instant.

"Click that button," the operator tells me. I do as I'm told.

In an adjacent building, four massive flywheels, spun up this morning using power from the local grid, release a 20-megawatt surge of electricity. The current energizes the ring magnets and charges up banks of beefy capacitors, preparing them for the huge zap to come. Within two minutes all the meters on my control screen have switched from "Preparing" to "Armed."

The operator leans into a microphone. "Triggering," he says over loudspeakers. Warning lights start flashing. I move the cursor to the button marked "Trigger." Then, I click it.

The capacitors release their pent-up electricity in a microsecond. Clouds of hydrogen ions form at the opposing ends of the vacuum cylinder and are propelled toward the center at nearly a million kilometers an hour. There they collide and form a hot, spinning plasma shaped like a giant, hollow cigar.

It sounds dramatic, but in the control room there is no flash, no roar—just a faint "ping," as if someone inside the reactor room had dropped a wrench onto the concrete floor. In an instant, the plasma blob has dissipated, and the computers have started processing the gigabyte of data streaming from dozens of sensors in the reactor. The warning lights switch off, and the workers return to their tasks.

Just another shot at fusion. When you fire as many as 100 shots a day, as Tri Alpha has been doing, one more is no big deal.

After 50,000 little pings in just two years, the C-2U test machine had by the time of my visit in February given the Tri Alpha team all the data it needed to move on. In April, Michl Binderbauer, the wiry, excitable physicist who is the company's chief technology officer, told his engineers to tear it down and cannibalize its parts for a more advanced reactor—dubbed C-2W—to be completed in mid-2017.

Tri Alpha's approach—build a prototype quickly, test it just enough and then trade up to a better one—is a striking departure from the norm in fusion research. For decades academic scientists have designed gargantuan machines intended to solve the mysterious behaviors in the fiery, pressurized plasmas that are supposed to create fusion reactions but often do not. Binderbauer, the son of a Viennese serial entrepreneur, exemplifies a new strain of fusioneer, driven by investors, an engineering mindset and an unwavering focus on building a practical power plant, not a monument to high-energy physics.

Several other start-ups, such as General Fusion outside Vancouver, are similarly betting that they can build a commercial machine without having to untangle every detail of the complex physics along the way. Such fusion power plants would run on fuels derived from ocean water or common minerals that are nearly inexhaustible and have no carbon. The plants would therefore produce almost no greenhouse gases. They also would pose virtually no radiation or weaponization risk and would generate enough electricity to run entire cities—all day, every day. All the new pioneers need to do is solve some of the hardest physics and engineering problems humans have ever tackled.

Right now the pragmatists have people's attention because the academics have hit practical dead ends: enormous reactors that have clarified some fusion science but are not on track to pump electricity into the grid by midcentury. One example is the National Ignition Facility (NIF) at Lawrence Livermore National Laboratory, a $4-billion machine that zaps tiny canisters of fuel with trillion-watt laser pulses. "NIF fires just a few hundred shots a year," Binderbauer says in his Austrian lilt. A power plant would have to fire tens of thousands of times a day. The system has delivered useful weapons research (its primary purpose), but its energy output would have to increase almost 30,000-fold just to cover what is required to run the lasers—and many times beyond that to be commercially useful. Two years ago Livermore pulled the plug on designing a prototype power plant.

The second discouraging example is ITER, a 10-story-high machine under construction in France by a consortium of nations. It will rely on giant superconducting magnets to control a plasma burning at roughly 150 million degrees C for minutes at a time. Even if it succeeds, ITER will make no electricity.

The politicians who launched ITER in 2006 expected it to cost

IN BRIEF

Major fusion projects such as ITER in France and NIF in the U.S. have consumed billions of dollars and are nowhere close to generating enough energy to even sustain their own operation, much less create commercial power. **Smaller, simpler designs** are now being explored, in some cases by private companies. Preliminary results have raised hopes that there might be more practical, less expensive paths to fusion power plants.

The newcomers face daunting scientific hurdles, however, such as preventing turbulence within superhot plasmas from snuffing out fusion reactions as soon as they start. Moving from brief experiments to the continuous, reliable operation needed for power plants raises formidable engineering challenges, too.

$11 billion and to be fully constructed this year. As of May, the cost had ballooned to $20 billion, with the U.S. on the hook for about $5 billion. Full operation will not come until 2035 at the earliest. Frustrated senators voted 90–8 to cut off U.S. funding. But after a subsequent though guarded vote of confidence by the U.S. Department of Energy, Congress was, at the time of this writing, poised to stay in the game, at least until next year.

Forewarned by the glacial progress of the giants, Binderbauer and the other mavericks are pinning their hopes on smaller machines that approach the problem from new angles. To deliver, they must compress a tiny amount of fuel densely enough, heated hot enough and confined that way long enough for atoms to fuse together, converting some of their minuscule mass into gobs of energy. NIF and ITER are at opposite ends of a spectrum of plausible designs that spans a huge range of plasma densities and energy-confinement times (a measure of how long heat stays inside the plasma). Most of the newcomers are searching for sweeter spots that lie in the less explored middle ground.

Equally important, the start-ups are designed to succeed or fail relatively quickly. Their reactors are "potentially 100 times less expensive than ITER, easier and faster to build, and lend themselves to faster research progress," says Scott Hsu, a fusion physicist at Los Alamos National Laboratory who works with HyperV Technologies, yet another start-up. (In this design, hundreds of guns fire bursts of argon plasmas into the center of a spherical reactor, where they converge and compress hydrogen fuel.) Any show-stopping flaws in these schemes most likely will show up well before the stakes rise to billions of dollars and decades of time.

That pleases their investors. General Fusion's $100-million bankroll has come in part from Amazon.com founder Jeff Bezos, the Canadian government and the sovereign wealth fund of Malaysia. Tri Alpha claims to have raised hundreds of millions of dollars from investors that include Goldman Sachs and Paul Allen, the co-founder of Microsoft. Another fast-moving group is Sandia National Laboratories, supported in part by the DOE's Advanced Research Projects Agency–Energy (ARPA-E), which funds long shots the way venture capitalists might do.

The backers are placing high-risk, high-payoff bets. Indeed, fusion research has been littered with cases where "nature says, 'nice idea, but it doesn't work that way,'" quips Stephen A. Slutz, who is the senior theorist on the Sandia project.

MICHEL LABERGE, founder and chief scientist of General Fusion, shows a diagnostic instrument that can help test unproved physics. "There's plenty of space to have a bad surprise—or a good one," he says.

SQUEEZING FIRE

THE CHALLENGE of stabilizing a furious plasma arises from the very nature of fusion itself. Two atomic nuclei, stripped of their electrons, can fuse only when they get close enough, for long enough, that the attraction of the strong nuclear force between them overcomes the electrostatic repulsion among the protons. When that happens, the ions merge to form a single nucleus of a heavier element that has less mass than the ingredients did. The missing matter transforms into bountiful energy, in the form of photons and fast-moving subatomic particles. Fission reactors, in contrast, extract energy from atoms such as uranium that are falling apart rather than joining together.

To get high rates of fusion, the ions in a plasma must be moving toward one another fast—but not too fast. That typically means a plasma temperature north of 100 million degrees C. A reactor must squeeze the superheated plasma into a relatively small space inside a vacuum chamber and hold the nuclei there until the reactions happen. As a rule of thumb, the product of the plasma's density and energy-confinement time has to be greater than about 10^{14} seconds per cubic centimeter. A wide combination of density, time and temperature can work.

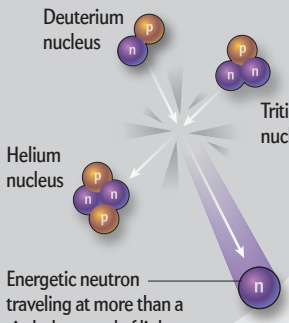
ITER, a "tokamak" reactor design, will use a wispy plasma of about half a gram of neutron-rich isotopes of hydrogen known as deuterium and tritium, floating within a vacuum chamber the size of a small house. ITER aims for a low plasma density, with energy confined for seconds at a time.

NIF, in contrast, trains up to 500 trillion watts of laser blasts from 192 directions onto a tiny canister encasing a frozen speck of solid deuterium and tritium. The optics and electronics that create and direct the laser pulses fill a building 30 meters high that is big enough to cover three football fields. To achieve ignition—a state in which the fusing fuel releases enough energy to sustain ongoing fusion reactions with no outside help—NIF seeks an incredibly high plasma density, which it needs because the energy is confined by inertia alone, for just a fraction of a nanosecond.

A big opportunity, says Patrick McGrath, ARPA-E's program director, may lie in the less explored regime between these two extremes: moderate plasma density and moderate energy-confinement times. But no machine has mastered the gremlins of turbulence and instability that inevitably appear in such plasmas. Controlling a hot plasma while fusion roars inside it is like trying to squeeze a candle flame without touching it—but even harder because the ions in a plasma generate their own complex and disruptive electric currents and magnetic fields. "Even if you can get the candle lit," says Dylan Brennan, a fusion scientist at the DOE's Princeton Plasma Physics Laboratory, "it blows itself out."

The New Fusion Reactors

Several bold groups are building prototype fusion machines that would convert tiny bits of matter into gobs of energy (*inset, left*). Sandia National Laboratories (*below*) and start-up General Fusion (*bottom right*) want to create hot plasmas that give off high-energy neutrons that can be converted into electricity. Tri Alpha Energy's approach (*top right*) would generate primarily x-rays that would be converted. The designs shown here are for commercial-style reactors.

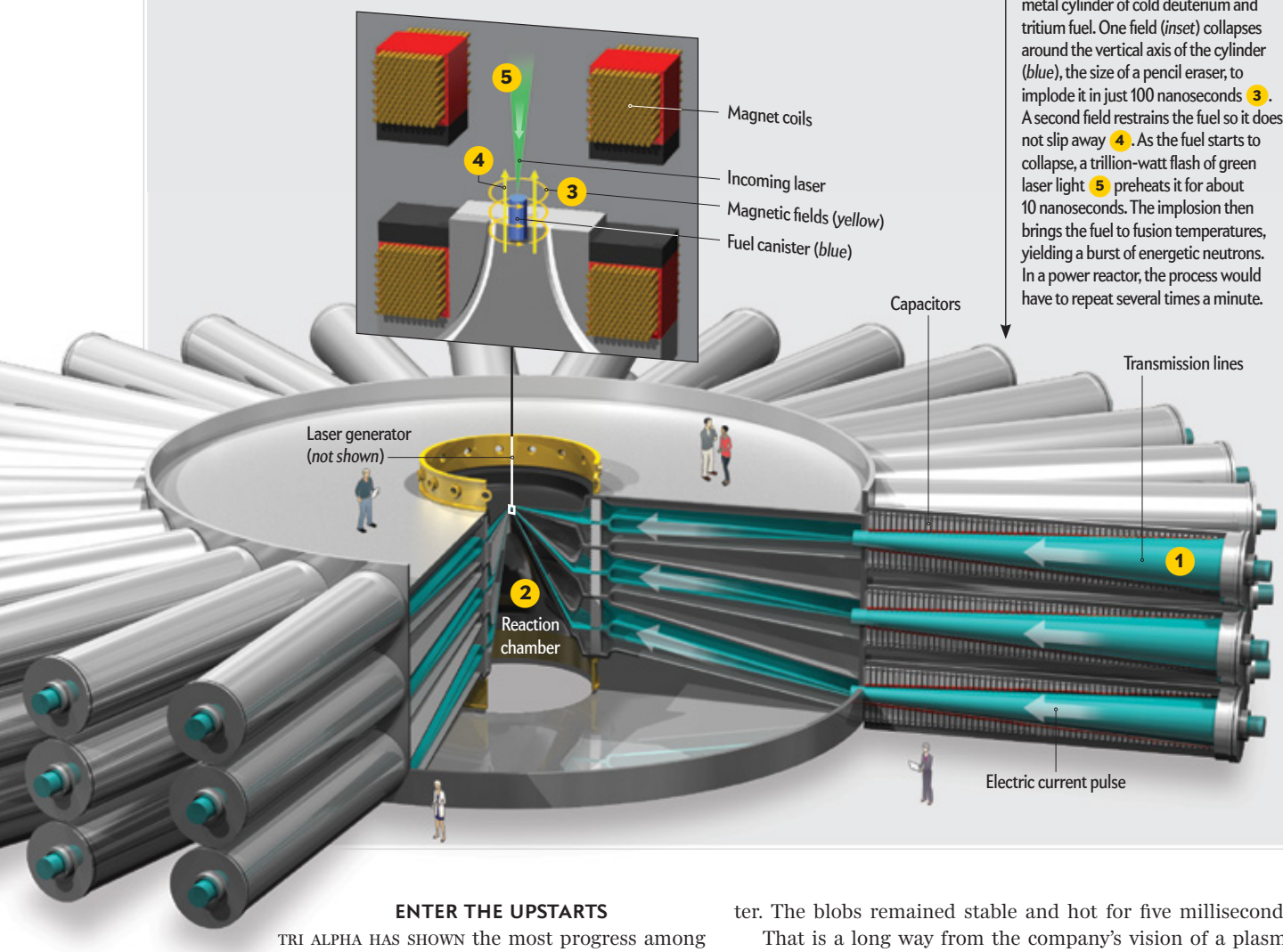


MATTER BECOMES ENERGY

When two ions (such as deuterium and tritium) collide at the right high speed, they fuse into a nucleus of a heavier element (such as helium) that has less mass than the two ions combined. The fusion converts the missing mass into energy, carried away by photons and fast-moving particles (such as neutrons).

SANDIA: BLAST THE FUEL

Ninety sets of capacitors and transmission lines (1) release a coordinated pulse of current, at 65 million amps, to the reactor chamber (2), creating powerful magnetic fields around a small metal cylinder of cold deuterium and tritium fuel. One field (*inset*) collapses around the vertical axis of the cylinder (*blue*), the size of a pencil eraser, to implode it in just 100 nanoseconds (3). A second field restrains the fuel so it does not slip away (4). As the fuel starts to collapse, a trillion-watt flash of green laser light (5) preheats it for about 10 nanoseconds. The implosion then brings the fuel to fusion temperatures, yielding a burst of energetic neutrons. In a power reactor, the process would have to repeat several times a minute.



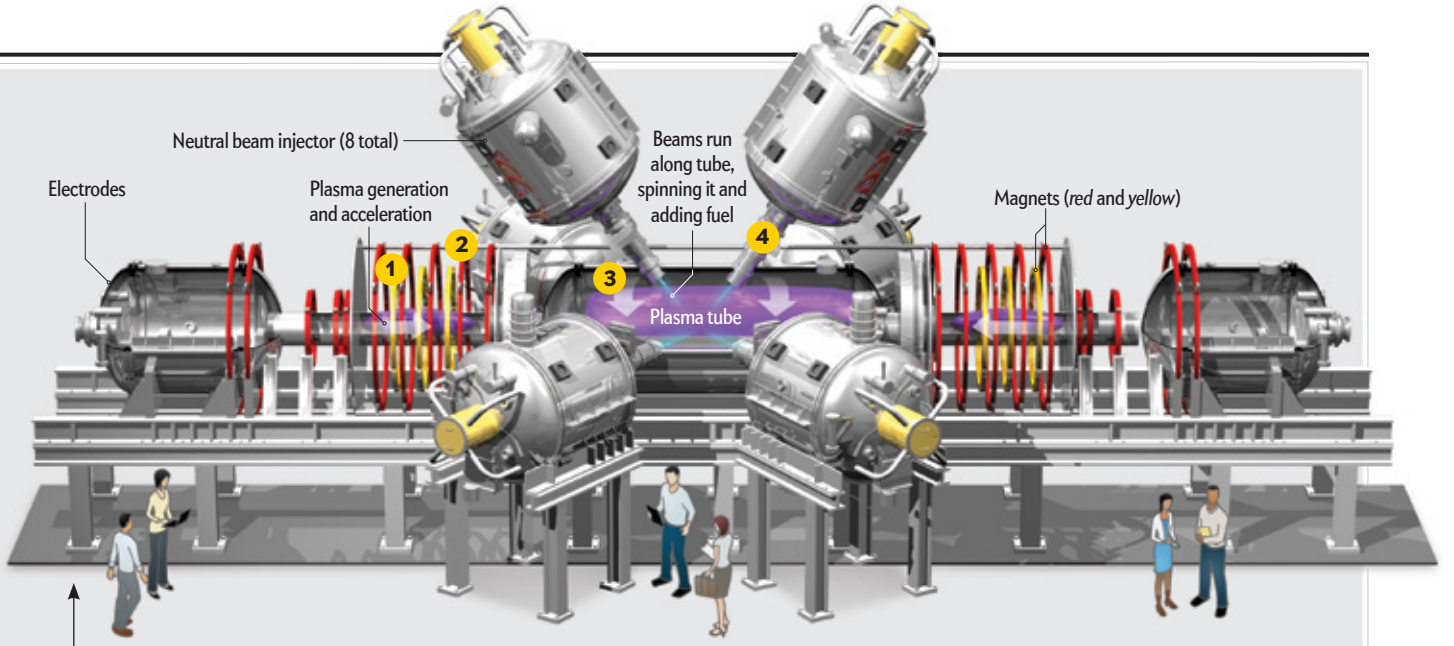
ENTER THE UPSTARTS

TRI ALPHA HAS SHOWN the most progress among the start-ups in maintaining a consistent grip on a plasma. "Everything you see here was built in less than a year," Binderbauer says proudly as we walk the 23-meter-length of the C-2U machine, tiny compared with NIF or ITER. Just three months after it turned on, it was creating up to 100 spinning blobs of hydrogen plasma a day, each having a density of about half the company's design goal of 10^{14} ions per cubic centimeter. The blobs remained stable and hot for five milliseconds.

That is a long way from the company's vision of a plasma that rotates quietly in place for days or weeks. But the tests were limited by the external power supplies. "Nothing says it can't go as long as we want it to," Binderbauer claims, in a full-scale reactor that powers itself as well as the grid. The upgraded C-2W will add digital feedback to counteract the tendency of the blob to wobble or drift.

Hsu, who has no affiliation with Tri Alpha, says the company

Illustrations by Don Foley (reactors) and Jen Christiansen (particle diagram)

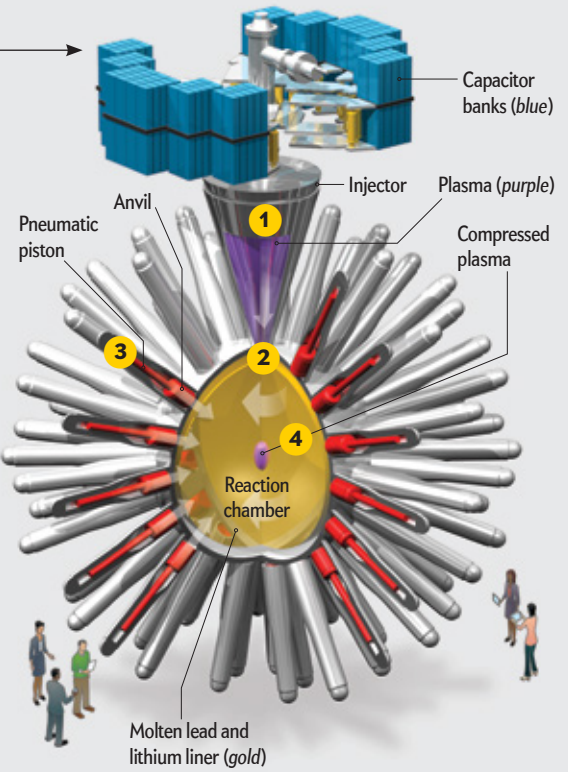


TRI ALPHA: SPIN THE IONS

A brief, intense jolt of electricity energizes magnets (*yellow*) on each side of the core (1), turning a puff of gaseous fuel into a plasma of boron ions and protons. Other magnets (*red*) hold the plasma in place while a huge, opposing magnetic field slams it for a microsecond, setting up a strong electric current inside the plasma (2). That circular current generates its own, bagel-shaped magnetic field, which acts like a cage to hold the plasma together. Another pulse of electricity is then sent through the first set of magnets, accelerating the plasma rings toward the center, where they slam into one another at roughly a million kilometers an hour. The collision forms a larger, hotter, tube-shaped plasma (3), which must reach 3.5 billion degrees Celsius for fusion reactions to take off. Eight injectors shoot beams of neutral atoms into the edges of the tube to keep it spinning around its axis (4), adding fresh fuel and stabilizing the plasma as it burns for hours or days at a time, giving off high-energy helium nuclei and x-rays.

GENERAL FUSION: SHOCK THE PLASMA

Capacitors power an injector that shoots a plasma of deuterium and tritium, shaped like a smoke ring, down a funnel (1), greatly compressing it before it enters the reaction chamber (2). There about 200 large pneumatic pistons smack simultaneously into anvils at 200 kilometers an hour (3), generating powerful shock waves. The waves speed through a vortex of molten lead and lithium that swirls along the inside wall of the chamber (4). When the waves converge at the center, the vortex implodes, compressing the plasma to about 150 million degrees C and a pressure greater than five million atmospheres, enough to initiate fusion for a fraction of a second. The liquid metal captures the neutrons and heat released by the fusion. The entire process would repeat once every second, generating bursts of energetic neutrons.



has achieved "tremendous progress. They have essentially solved the stability problem." But demonstrating longer containment times—and at far higher temperatures, while pumping in a steady stream of fuel—will be crucial because the reactor must run continuously to generate power.

General Fusion's reactor, in contrast, works in pulses. The spherical, steel reaction chamber, erected inside a suburban warehouse, is a meter across and bristles with pistons a third of a meter wide, each nearly as long as Michel Laberge, the company's tall, red-bearded founder and chief scientist. Laberge describes the steampunk-looking machine in a pronounced French-Canadian accent: "Compressed gas accelerates these pistons to 200 kilometers an hour, and then they hit anvils—bang!" he shouts as he claps his hands loudly. "The impacts all have to occur within five microseconds to create a shock wave" that collapses at the exact center of the chamber.

When all the machine's pieces are integrated, they will fire once every second, like a beating heart. With each beat, a smoke

ring of plasma squirted into the sphere will compress and set off a brief but energetic cascade of fusion reactions. It is easier to manage turbulence using this pulsed approach, Laberge argues, because each little doughnut of plasma has to remain stable for only a millisecond or so.

Laberge says the injector system has already produced plasmas having the right preimplosion density, as well as the necessary temperature and magnetic field strength. But the plasmas lasted only 20 microseconds—50 times too short—before falling victim to instability. Laberge is confident that a new nozzle design, shaped more like the bell of a trumpet, will twist the magnetic field that the plasma itself creates by just the right amount to hold the fuel together long enough to fuse.

And yet "a lot of people in the field say that General Fusion's approach is never going to work," notes Brennan, who is helping the company. The critics doubt that a small group of people in a start-up can master plasma problems that have frustrated academic researchers for years. "But scientifically, do we have the answer that tells us they can't do it?" Brennan asks. "No."

Half a continent away in New Mexico, experiments with a technique called MagLIF at Sandia have accomplished what the start-ups have yet to do: create appreciable amounts of fusion. Like NIF, MagLIF aims for high ion densities—around 10^{24} ions per cubic centimeter—and energy-confinement times of mere nanoseconds. But the Sandia system is, at 34 meters across, far smaller and much less expensive than NIF because it uses a one-two punch to heat and pressurize fuel trapped inside a cylinder no bigger than the eraser on a pencil.

The so-called Z machine that feeds MagLIF unleashes a 19-million-amp electrical jolt that exerts a powerful magnetic pinch, crushing the cylinder. A brief trillion-watt laser blast ionizes the fuel as it starts to implode. The machine imposes a separate magnetic field to keep the resulting plasma from squirting out the ends of the cylinder. But the collapsing cylinder can develop instabilities that allow fuel to escape through the sides.

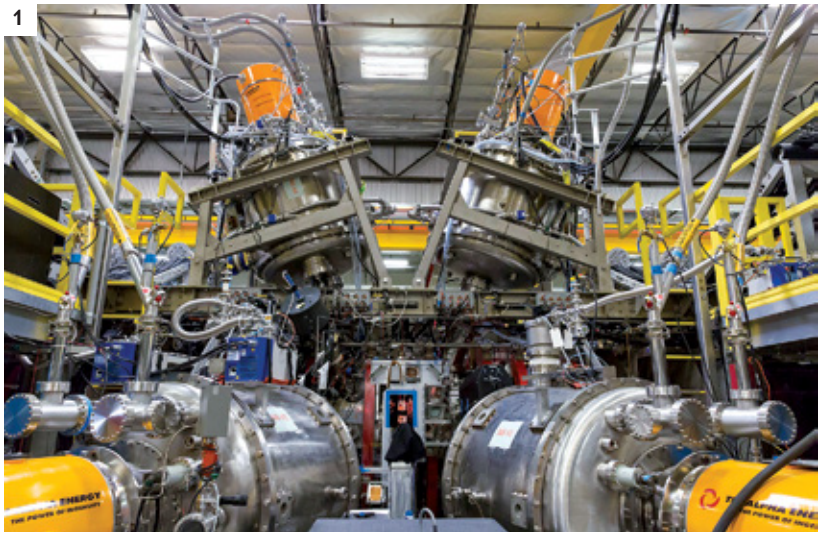
The amount of fusion generated in each MagLIF shot has soared 100-fold since tests began in late 2013. "MagLIF works pretty darn well already," Hsu says. Daniel Sinars, the project leader, says he expects even better results from shots scheduled for late 2016.

If all goes well, the team plans to boost the electrical jolt to 25 million amps. That should generate around 10^{16} fusion reactions, enough to offset the energy absorbed by the fuel on its way to fusing, matching NIF's 2014 achievement at a mere fraction of the cost. "That would be very exciting," Sinars says.

Sandia is already drawing plans to upgrade the Z machine. With 65 million amps and the addition of tritium to the deuterium fuel used thus far, the new Z800 could generate up to 100,000 times more energy per shot. Is that enough to achieve ignition, reaching self-sustaining fusion a decade or more before ITER will? Sandia researchers calculate that it might be.

Because Sandia is a national lab, Congress would have to approve any major upgrade, and it has not been in a spending mood. But competition could change that sentiment. According to Slutz, Chinese scientists have already constructed a smaller version of Z and are replicating Sandia's published experiments, and Russia is planning to build a similar 50-million-amp machine.

1



COURTESY OF TRI ALPHA ENERGY, INC.

TURNING UP THE HEAT

IF ANY OF THESE FUSION SCHEMES succeeds in reaching the necessary ion density and confinement time, it still must supply the third ingredient required for ignition: an incredibly high plasma temperature. Doing that is hard because light emissions, electron interactions and myriad other mechanisms can cool the plasma enough to snuff out fusion reactions soon after they start.

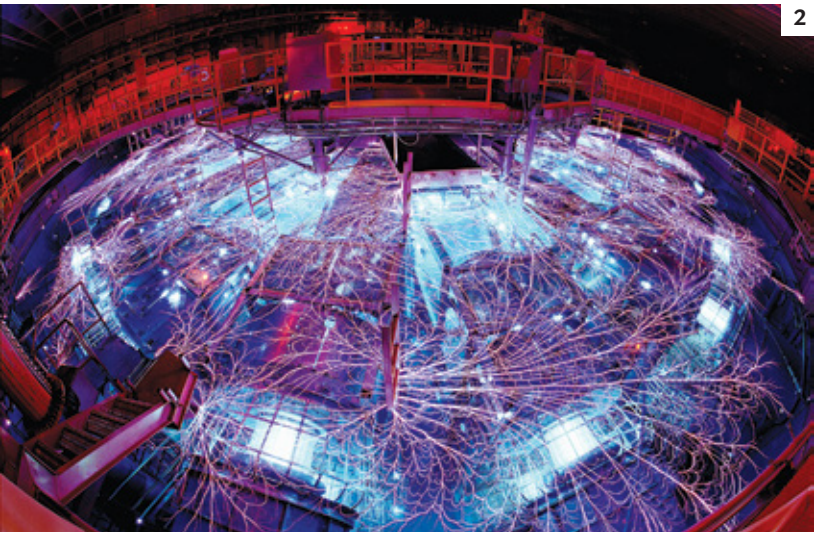
At Sandia, for example, Sinars and Slutz have been scratching their heads over why the laser has not been heating the fuel nearly as much as their models predict. The thin window that covers the open end of the fuel target may be scattering the light. But a laser may simply be the wrong tool for the job. For a commercial system, "you probably would want to heat the fuel some other way," Sinars admits. The team is trying to improve laser heating, but if it cannot, the failure at least will have come early in the game.

Tri Alpha has to reach a far higher temperature than its competitors because it is using a fuel blend of protons and boron 11, which burns at 3.5 billion degrees C. That is more than 20 times hotter than needed for deuterium-tritium fuel.

Hotter plasmas tend to be harder to contain. But Binderbauer is betting that Tri Alpha's energy confinement will actually improve as the temperature soars. It has in experiments thus far, but even the new C-2W machine will heat plasmas to just a fraction of 1 percent of the needed temperature and hold them for just 30 milliseconds. Binderbauer concedes that he could lose this bet on physics but says "we don't have data in this regime. We have to go prove it."

General Fusion must struggle with unproved physics, too—notably, how fast heat escapes from the plasma. "This cannot be calculated from first principles, so there's plenty of space to have a bad surprise—or a good one," Laberge says. "If the [heat] losses are worse than expected, we can make the machine bigger. But if it grows to be the size of ITER, then we have a problem."

SCIENTIFIC AMERICAN ONLINE For more on competing reactor designs, go to ScientificAmerican.com/nov2016/gibbs



2

INJECTORS (*yellow* and *silver*) at Tri Alpha (*1*) fire atomic beams that would spin a hot fusion plasma to keep it stable inside a reactor core. The Z machine at Sandia (*2*) generates short pulses of intense current that would create strong magnetic fields to compress fusion fuel.

COURTESY OF RANDY MONTOYA *Sandia National Laboratories*

FROM PROTOTYPE TO POWER PLANT

CHAMPAGNE CORKS WILL POP the day some reactor achieves ignition—and then a long slog of hard engineering work will begin to transform an experimental reactor into a power plant that generates both electricity and profits. To make a dent in the global electricity supply, which is forecast to grow 70 percent by 2040, fusion will have to compete on cost with other clean energy options.

Giant tokamaks like ITER probably will never succeed, says Dennis Whyte, who directs the Plasma Science and Fusion Center at the Massachusetts Institute of Technology, because they eat up too much of their own power to function. The start-ups have put more thinking up-front into engineering but will still face numerous practical challenges.

For the foreseeable future, for example, each MagLIF shot at Sandia will destroy part of the equipment. Deuterium-tritium fusion releases most of its energy as high-speed neutrons, which damage steel parts and gradually turn them radioactive. Any fusion plant that uses this kind of fuel will have to capture the fast neutrons and use their heat to spin turbines that generate electricity while minimizing the side effects. Scientists there are not dwelling yet on how to prevent the damage, and they have only rough and untested notions of how they might quicken the shot rate from several a week to several a minute. HyperV and Magneto-Inertial Fusion Technologies, a small company in Tustin, Calif., are using money from ARPA-E to explore related schemes that might solve some of these issues, but these efforts are not nearly as far along.

Tri Alpha is pursuing proton-boron fusion precisely to avoid the headaches that come with fast neutrons. Fusion with this fuel emits three helium nuclei, known as alpha particles—hence the company's name—and x-rays but hardly any neutrons. The downside: the x-rays carry over 80 percent of the energy produced.

In principle, Binderbauer says, photovoltaic cells lining the interior of the vessel could convert those photons into electricity. But that technology does not yet exist. So the company is exploring the idea of running coolant along the interior wall of the fusion chamber to extract heat deposited by the x-rays.

General Fusion is sticking with deuterium-tritium fuel, despite the neutron issue and the fact that tritium is mildly radioactive, exceedingly rare and very costly. Laberge plans to pump a swirling vortex of molten lead and lithium along the interior walls of the reaction chamber to capture the neutrons' energy. The neutrons will also split some of the lithium atoms into helium and tritium, which can then be recycled as fuel.

It is an elegant solution on a whiteboard, but no one has ever built such a system. The amount of tritium that would be bred is still speculative, Hsu says. And Laberge worries that as shock waves from the pistons pass through the lead-lithium mixture, some of the metal could spray into the plasma, squelching the fusion. "It would be like pouring water on fire," he concedes.

ROADS LESS TRAVELED

GIVEN THE DISAPPOINTING PACE at ITER and NIF, Whyte says, "the time is ripe to take all of the science we've built up and look at other optimizations," including riffs on tokamaks that make them smaller or twist them into odd shapes called stellerators. "I would love to see a race between a very compact tokamak, General Fusion's idea, a compact stellarator and a machine like Tri Alpha's. Let's see what works best."

Currently that race in the U.S. is relying on the kindness of investors. Federal money for alternative paths to fusion has been dwindling year by year, Hsu notes. He and Stewart Prager, head of the plasma physics lab at Princeton University, have urged Congress to increase research funding to explore innovative fusion concepts, which could allow other ambitious start-ups to rise to the challenge. If any of the innovative concepts are successful, Hsu says, "fusion energy could possibly be developed for a few billion dollars in less than 20 years."

Maybe, maybe not. As Binderbauer points out, "there's plenty of opportunity for the physics we don't yet know to bite us in the ass."

But consider the potential payout: a new source of energy that doesn't rely on the whims of the wind or sun blocked by clouds, wouldn't require big changes to the existing electrical grid, doesn't raise concerns about nuclear weapons, can't melt down or irradiate surrounding communities, and might be no more expensive, after it gets going, than other forms of clean energy.

Is it worth taking a few more shots? SA

MORE TO EXPLORE

Plasma Physics: The Fusion Upstarts. M. Mitchell Waldrop in *Nature*, Vol. 511, pages 398–400; July 24, 2014.

Scaling Magnetized Liner Inertial Fusion on Z and Future Pulsed-Power Accelerators. S. A. Slutz et al. in *Physics of Plasmas*, Vol. 23, No. 2, Article No. 022702; February 2016.

FROM OUR ARCHIVES

Fusion's False Dawn. Michael Moyer; March 2010.

scientificamerican.com/magazine/sa

5 THINGS WE KNOW TO BE TRUE

A COMPENDIUM OF IRREFUTABLE FACTS FOR THESE FACT-STARVED TIMES

SCIENTIFIC TRUTHS are always provisional at some level. We once believed that the continents were fixed on the surface of Earth; now we know they move. We thought the universe was static; now we know it's expanding. We thought margarine was healthier than butter and that hormone-replacement therapy was the right treatment for vast numbers of postmenopausal women; now we know better.

But while scientists do not know everything, there is plenty they

Illustrations by Red Nose Studio

IN BRIEF

In election years, the small but vocal contingents that refuse to accept scientific consensus on certain issues tend to get louder.

We thought this would be a good time to clearly and emphatically lay out the case for several well-established—but, in some circles, strangely contentious—scientific truths.

Consider this a cheat sheet for debates with the antiscience crowd.

do know. And especially during this political season, it is dispiriting to see how many people—including political candidates—bizarrely reject some of the most basic, evidence-based truths that underlie modern science.

We ordinarily report on the latest advances in scientific and technological research, but we thought it appropriate to take a step back and discuss some of science's firmly established facts. There is essentially no debate among legitimate scientists about these truths, which are based on verifiable evidence, which have been accepted for decades and which have only become more strongly established as new evidence continues to accumulate.

Psychological research has shown that being confronted with that mounting evidence can actually harden the positions of the truth deniers, so we do not pretend that the essays that follow will fix the problem. Nevertheless, we feel it is our duty to point out that some things actually are true, even in the constantly growing and evolving world of science. *—The Editors*

MONSTERS, INC.—Bigfoot, the Loch Ness monster and similar creatures do not exist. The idea that large, unknown animals roam the woods of the Pacific Northwest, glide through chilly Scottish waters and hike the Himalayas is eerily appealing, but the evidence is basically zero.

Evolution Is the Only Reasonable Explanation for the Diversity of Life on Earth

BY MICHAEL SHERMER

ON JANUARY 14, 1844, CHARLES Darwin wrote a letter to his friend Joseph Hooker, recalling his voyage around the world on the HMS *Beagle*. After five years at sea and seven years at home thinking about the origin of species, Darwin came to this conclusion: "At last gleams of light have come, & I am almost convinced (quite contrary to opinion I started with) that species are not (it is like confessing a murder) immutable."

Like confessing a murder. Dramatic words. But it doesn't take a rocket scientist—or an English naturalist—to understand why a theory on the origin of species by means of natural selection would be so controversial. If new species are created naturally—not supernaturally—what place, then, for God? No wonder that more than a century and a half later people of some religious faiths still find the theory so terribly threatening. But in those intervening years scientists have found so much evidence in support of the theory that it would be truly astonishing if it turned out not to be true—as shocking as if the germ theory of disease fell apart or if astrophysicists were forced to abandon the big bang model of the universe. Why? Because of a convergence of evidence from many lines of inquiry.

For example: Comparing data from research in population genetics, geography, ecology, archaeology, physical anthropology and linguistics, scientists discovered that Australian Aborigines are genetically more closely related to South Asians than they are to African blacks—which makes sense from an evolutionary perspective because the migration pattern of humans out of Africa led them to Asia and then to Australia.

The consistency of dating techniques also gives us confidence that the theory is true. Uranium-lead, rubidium-strontium and potassium-argon dating, for example, are all reasonably consistent in their determination of the age of rocks and fossils. The ages are given in estimates, but the margins of error are in the range of 1 percent. It is not as if one scientist finds that a fossil hominin is 1.2 million years old while another one finds it is 10,000 years old.

Not only are the dates consistent, but the fossils also show intermediate stages—something antievolutionists still insist don't exist. There are now at least six intermediate fossil stages in the evolution of whales, for instance, and more than a dozen fossil hominins, several of which must have been intermediate with humans since the hominins branched off from chimpanzees six million years ago. And geologic strata consistently reveal the same sequence of fossils. Trilobites and mammals are separated by many millions of years, so finding a fossil horse in the same geologic stratum as a trilobite—or even more drastically, a fossil hominin in the same stratum as a dinosaur—would prove problematic for the theory of evolution, but that has never happened.

Finally, vestigial structures are signs of evolutionary history. The Cretaceous snake *Pachyrhachis problematicus* had small hind limbs, which are gone in most of today's snakes. Modern whales retain a tiny pelvis for hind legs that existed in their land-mammal ancestors. Likewise, flightless birds have wings. And of course, humans are replete with useless vestigial structures—a distinctive sign of our evolutionary ancestry—such as wisdom teeth, male nipples, body hair, the appendix and the coccyx.

As the great geneticist and evolutionary theorist Theodosius Dobzhansky famously noted, "Nothing in biology makes sense except in the light of evolution."

Michael Shermer is publisher of *Skeptic* magazine, a monthly columnist for *Scientific American* and a presidential fellow at Chapman University. His latest book is *The Moral Arc*. Follow him on Twitter @michaelshermer

GMOs ARE NOT SCARY—"Frankenfoods" sound like a terrifying concept, but despite extensive testing, genetically modified organisms have never been shown to be dangerous.

100% BS—No, we do not use only 10 percent of our brainpower. Nobody knows where this "fact" even came from, but it's nonsense.

Homeopathy Has No Basis in Science

BY HARRIET HALL

HOMEOPATHY IS A SYSTEM OF medicine that purports to treat disease with minute doses of substances that in a healthy person would produce symptoms of that disease. It is based on the unscientific thinking of a single misguided individual, a German doctor named Samuel Hahnemann, who invented it in the early 1800s.

Homeopathy not only doesn't work; it couldn't possibly work. It is inconsistent with our basic knowledge of physics, chemistry and biology. Oliver Wendell Holmes thoroughly debunked it in 1842 with his essay "Homeopathy and Its Kindred Delusions." He would have been appalled to think anyone could still believe it in 2016.

Few users of homeopathy have bothered to inform themselves about what they are taking or the wacky ideas behind it. The simplest way to explain homeopathic theory is with this example: If coffee keeps you awake, dilute coffee will put you to sleep—the more dilute, the stronger the effect. If you dilute it until there isn't a single molecule of coffee left, it will be even stronger. (The water will somehow remember the coffee that is no longer there.) If you drip the coffee-free water onto a sugar pill and let it evaporate, the memory of coffee will be transferred to the sugar pill, and the pill will relieve insomnia.

If any of that makes sense to you, you should be worried.

You wouldn't think anyone would buy a medicine that contained no active ingredient, but they do. A product called Oscillococcinum is sold in most American pharmacies, bringing in an estimated $15 million a year from customers hoping to relieve the symptoms of flu and colds. The name is that of the oscillating bacteria that a French physician, Joseph Roy, imagined he could see in the blood of flu victims and in duck liver; no one else ever saw them. The box says the active ingredient is *Anas barbariae* 200 CK HPUS. That means Muscovy duck (the heart and liver), and it means they diluted it 1:100 and repeated that process 200 times, "succussing" it after each dilution (it is shaken, not stirred). Any chemistry student can use Avogadro's number to calculate that by the 13th dilution, there is only a 50–50 chance that a single molecule of duck remains, and by the 200th dilution the duck is history. All that remains is the quack.

Homeopaths' prescribing methods are unbelievably silly. They ask a laundry list of irrelevant questions (What color are your eyes? What foods do you dislike? What are you afraid of?). They consult two books. The first is a *Repertory* listing remedies for every possible symptom—for example, clairvoyance (yes, it considers this a symptom), dental caries and "tearful" (sic). The second is a *Materia Medica* listing the symptoms associated with each remedy ("dreams of robbers" are linked to table

Harriet Hall is a retired family physician who writes about medicine, alternative medicine, science, quackery and critical thinking. She is one of the founders and editors of the Science-Based Medicine blog, a fellow of the Committee for Skeptical Inquiry and a board member of the Society for Science-Based Medicine.

THIS IDEA IS ALL WET—You do not need to drink eight glasses of water a day. You do have to replace fluids lost to urine and perspiration, but some comes from food, and there's no set amount.

EXPENSIVE URINE—Unless you have a deficiency or no access to healthy food or a balanced diet, vitamin supplements are pretty much a waste of time and money.

salt!). Yes, dilute table salt and pretty much anything imaginable can be a remedy. Some of my favorites: Berlin wall, eclipsed moonlight, dog's earwax and the south pole of a magnet. It's absurd, but an estimated five million adults and one million children use homeopathic remedies every year in the U.S., mostly self-prescribed and purchased in a pharmacy.

Even though there are published studies claiming that homeopathy works, you can find a study to support almost anything, and rigorous scientific reviews of the entire body of research have consistently concluded that it works no better than placebos. As Edzard Ernst, emeritus professor of complementary medicine at the University of Exeter in England, and author Simon Singh have written, "The evidence points towards a bogus industry that offers patients nothing more than a fantasy."

The FDA allows the sale of homeopathic remedies under a "grandfather" clause exempting them from the requirement to demonstrate effectiveness, but it is considering changes in regulation. I wish they would require a label stating, "Contains no active ingredient. For entertainment purposes only." The persistence of homeopathy demonstrates the inability of the general public to think critically. People have used homeopathy instead of effective drugs, vaccines and malaria prophylaxis, with disastrous results. People have died.

Homeopathy was bunk in 1842, and it remains bunk today. By now we ought to know better.

Climate Change Conspiracy Theories Are Ludicrous

BY RAY PIERREHUMBERT

I AM ALWAYS BAFFLED THAT SOME people have convinced themselves that the scientific consensus underpinning anthropogenic global warming is a vast conspiracy to destroy the American way of life, foist socialism on the unsuspecting masses, or … insert your favorite gripe here.

If it is a conspiracy, it is a truly remarkable one, spanning nearly two centuries and the scientific communities of dozens of nations. The foundations of our understanding of planetary temperature begin with the work in the 1820s of French physicist Joseph Fourier, who established that a planet's temperature is determined by the balance between energy received from the sun and infrared radiation emitted back into space. Quantification of Fourier's basic idea depended on the development of blackbody radiation theory by Austrian Ludwig Boltzmann in the mid-1800s and his German contemporary Gustav Kirchhoff. Irish-born physicist John Tyndall brought carbon dioxide into the picture in the late 19th century by showing that it traps infrared radiation, and Swedish chemist Svante Arrhenius put it all together shortly thereafter.

There were many later developments in the 20th century, culminating in a quite complete theory incorporating both carbon dioxide and water vapor feedback, which Syukuro Manabe developed while working at NOAA's Geophysical Fluid Dynamics Laboratory in the 1960s and 1970s. We have learned plenty since then, but Manabe basically nailed it. Our understanding of the connection between greenhouse gases and global warming rests on the same principles that underlie heat-seeking missiles, weather satellites and infrared remote controls. It would take quite a conspiracy to fake all that.

It would take an even greater conspiracy to fake the changes in Earth's climate that theory predicts and scientists have observed, including higher global average temperatures, rising sea levels, dwindling ice in the Arctic and Antarctic, melting glaciers, increases in the intensity and duration of heat waves, and more. The cabal would also have to fake all the data from past climates that tells us there is no magic mechanism (clouds or otherwise) that will save us from the well-established warming effects of carbon dioxide acting in concert with water vapor. It would have to fake the observations that tell us that subsurface ocean waters are warming—evidence that the energy that is heating the planet's surface is not coming from the oceans. (Energy is conserved, so if the oceans were causing surface warming, then they would be cooling down in response. Conservation is not just a personal virtue—it's the law!) Likewise the carbon isotope and carbon budget data that prove that the carbon dioxide accumulating in the atmosphere really does come from deforestation and burning fossil fuels. It would have to fake the observed conjunction of stratospheric cooling with tropospheric warming, which is characteristic of the influence of carbon dioxide and other long-lived greenhouse gases on the atmosphere.

And so on and so forth. It adds up to an awful lot of stuff to fake and makes faking the moon landing look like a piece of cake.

Science rewards those who overturn previous dogma (think quantum theory versus classical mechanics), so the fact that the basic theory of anthropogenic global warming has weathered all challenges since appearing in its modern form in the 1960s is saying a lot. Global warming is a problem, and we caused it. That's still true even if Donald Trump disagrees. Arguing about the basic existence of the problem has no place in a sane discourse.

Ray Pierrehumbert is Halley Professor of Physics at the University of Oxford.

DON'T FALL OFF THE EDGE—No, just kidding. Earth is not flat. Christopher Columbus knew it when he set sail. You know it, too. Or most of you do, anyway.

NO FREE LUNCH—Free energy and perpetual motion sound great. But thermodynamics says no way, and that's the law.

Vaccines Do Not Cause Autism

BY PAUL OFFIT

IT HAS BEEN ALMOST 20 YEARS since a paper published in the *Lancet* gave birth to the notion that vaccines caused autism. Since then, more than two dozen studies have refuted the claim, and the original paper has been retracted.

For the most part, the money and time devoted to studying the vaccine-autism hypothesis have been worth it. First, media outlets no longer carry this story under the false mantra of balance, telling two sides when only one is supported by the science. Now the story is one of a disproved claim proposed by a discredited doctor. Second, most parents no longer believe that vaccines cause autism. A recent study showed that 85 percent of parents of children with autism do not believe that vaccines were the cause.

Unfortunately, despite the mountain of evidence refuting the association, a small group of parents still believe that vaccines might cause autism. Their failure to vaccinate their children not only endangers the children but also weakens the "herd immunity" that keeps disease outbreaks contained. There are several plausible reasons why they feel this way.

One possibility is that the cause or causes of autism remain unknown—the same situation that applied to diabetes in the 1800s, when no one knew what caused it or how to treat it. At the time, people proposed a variety of crazy causes and heroic cures. Then, in 1921, Frederick Banting and Charles Best discovered insulin, and all these false beliefs melted away. Until a clear cause and cure for autism emerge, the vaccine hypothesis will be hard to put completely to rest.

Another possibility is that the notion that vaccines cause autism is comforting—certainly far more comforting than studies that have shown a genetic basis. If autism is caused by events occurring outside the womb, then parents can exercise some form of control. If the disorder is genetic, there is no control.

And everyone loves a bogeyman. It is nice to be able to point a finger at an evil force causing autism, especially if it is big pharma or big government. Conspiracy theorists argue that the only reason studies have shown that vaccines do not cause autism is that a vast international conspiracy is hiding the truth. Although only a small group of parents hold this belief, their voices are disproportionally represented on the Internet.

Finally, parents of children with autism often perceive them as developing normally up to about 12 months of age. Then, after receiving a series of vaccines, the child misses speech, language, behavior and communication milestones typically seen in the second year of life. In fact, several studies examining videotapes taken in the first year of life show that these children were not developing normally. But from the parents' perspective, they were.

The most encouraging aspect of the vaccine-autism controversy has been the emergence of academics, clinicians, public health officials and parents who have taken to the Internet, the airways and the print media to represent the science that has exonerated vaccines. As a consequence, the tide has turned. We now hear the voices of parents who are angry that other parents, by choosing not to vaccinate, have put all children at risk.

This societal outcry in favor of vaccines was made all the more immediate by the 2015 measles outbreak, which began at the Disney theme park in southern California and spread to 189 people, mostly children, in 24 states and the District of Columbia. Unfortunately, nothing educates better than the virus. Invariably, it is the children who suffer our ignorance.

Paul Offit is a professor of pediatrics in the Division of Infectious Diseases and director of the Vaccine Education Center at the Children's Hospital of Philadelphia.

CRIME SEEN—Or rather, not seen. Criminal activity does not increase during the full moon. It can seem that way, even to police officers, because you notice things that confirm your expectations. But despite a handful of suspicious-looking studies, most research says the idea is lunacy.

RATATOUILLE—Treatso in humans. Animal tests hear that a cure based on

SCIENTIFIC AMERICAN ONLINE The presidential candidates answer science questions at ScientificAmerican.com/nov2016/sciq

ing cancer in rodents is not the same as doing have led to many new treatments. But if you rodents is on the way, you should smell a rat.

SA

No Credible Evidence of Alien Visitations Exists

BY SETH SHOSTAK

MILLIONS OF PEOPLE IN THE U.S. claim they have been abducted by aliens, according to a 2013 story in the *Washington Post*. That's an impressive tally for the aliens. And yet the government's response has been tepid. That should tell you something: either the Feds think it's not happening, or they're part of the problem.

Many people believe the latter. They say that the government knows the aliens are here but keeps the evidence under wraps at Area 51 or some other top-secret venue.

But hold on.

Unless extraterrestrials prefer Americans (and exceptionalism aside, why should they?), then the rate of abduction worldwide shouldn't be terribly different from what it is here. Assuming an aliens-without-borders effort, tens of millions of folks around the world have been grabbed by the grays. I think the United Nations would notice. I think you'd notice.

Abductions, of course, are only one component of the so-called UFO phenomenon. The majority of the evidence is composed of sightings—eyewitness accounts, photos and videos. Most of these can be explained as aircraft, rockets, balloons, bright planets or, occasionally, hoaxes. Some remain unexplained—but that only means they're *unexplained,* not that they're flying saucers, no matter how convinced the people who report them might be. There remains no scientifically validated evidence that extraterrestrials have been here, either recently or in the distant past. The pyramids, the Nazca lines in Peru and all the other artifacts that have been ascribed to ancient astronauts can be straightforwardly explained by human activity.

In fact, few scientists or science museum curators feel that the claim we're being visited is even plausible. Even aside from the formidable technical challenges of interstellar travel, ask yourself this: Why are they here now? *Homo sapiens* has only been broadcasting its presence to the universe since the advent of television and radar. Unless the extraterrestrials come from a very close star system, there has not been adequate time for them to learn of our existence and fly to Earth. Even if they could get here at the speed of light (which they couldn't), they'd have to live within 35 or so light-years of us—and there aren't all *that* many close stars. Besides, high-speed space travel takes an enormous amount of energy. Would you pay a gargantuan utility bill just for a little "catch and release" sport-fishing for hominins?

Nevertheless, for decades polls have shown that roughly one third of the populace believes our world is host to cosmic visitors. If despite the lack of good evidence, you insist on believing this is true, you also have to admit they are the best guests you could ever have. They don't kill us, they don't foment unrest, they don't steal the silverware. The Roswell incident was nearly 70 years ago. If aliens have been here since, they deserve good conduct medals.

Seth Shostak is senior astronomer at the SETI Institute, a nonprofit organization that studies the nature of life beyond Earth. He also co-hosts a weekly radio program, *Big Picture Science*.

MORE TO EXPLORE

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EVOLUTION

Species IN THE Making

Killer whales appear to be splitting into several separate species, perhaps because cultural differences among populations are driving them apart

By Rüdiger Riesch

Rüdiger Riesch is a lecturer in evolutionary biology at Royal Holloway, University of London. His research focuses on the mechanisms that create, maintain and constrain biodiversity, with a special emphasis on speciation that occurs as a result of a population exploiting a new ecological niche.

JUST OFFSHORE FROM THE PEBBLE BEACHES OF BERE POINT ON MALCOLM ISLAND, British Columbia, the *Naiad Explorer* rocks gently in the waters of the Queen Charlotte Strait. The sun has burned off most of the morning mist, save for a thin layer that still shrouds the tips of the island's cedars, firs and spruces. I watch from the boat as three killer whale brothers named Cracroft, Plumper and Kaikash gently scrape their bodies against the small, smooth stones in the shallows off the bow. The brothers have already spent the better part of an hour here absorbed in this activity. Soon they will leave to hunt for salmon or look for mates.

Exactly why the creatures engage in this scraping behavior, known as beach rubbing, is uncertain. Most experts assume that it aids in sloughing off dead skin and dislodging external parasites, but it might also be for pleasure. Whatever the motivation behind it, beach rubbing, though rarely observed in other cetaceans—the group that includes whales, dolphins and porpoises—is commonplace here. It is part of the distinctive cultural fabric of the northern resident killer whales, a community that claims the waters around northern Vancouver Island as home during the summer months. (Despite their name, killer whales are actually large dolphins.)

The northern resident killer whales are not the only ones with unique behaviors. Observations made since the 1970s have shown that killer whale populations around the globe each have unique ways of doing everything from hunting to communicating. Physical traits, including coloration, body size and dorsal fin shape, vary among groups as well, albeit somewhat more modestly. These cultural and physical differences, along with the astonishing degree of genetic diversity documented in these creatures over the past 15 or so years, suggest to me and many other researchers that today's killer whale populations, rather than simply representing the single species scientists have long envisioned, are actually in the midst of going their separate evolutionary ways. That is, they appear to be splitting into new species that, if this process continues, ultimately will be unable to produce viable or fertile offspring with one another.

Intriguingly, their cultural differences may be driving this diversification: the whales seem to mate with individuals that largely share their customs, to the exclusion of those that do not, a preference that creates the conditions needed for speciation to occur. If so, then killer whales could provide a striking example of a speciation mechanism not considered in the classical theory of how new species arise. They might also offer insights into how another group of creatures—*Homo sapiens* and our extinct predecessors—diverged into an array of species that once shared the planet.

A DIVERSITY OF KILLERS

FOR MORE THAN A CENTURY biologists have looked to geography to explain how speciation occurs. In the favored scenario, called allopatric speciation, two populations of an ancestral species

IN BRIEF

Evolutionary biologists have long turned to geography to explain the emergence of new species.
In the classic explanation, two populations of an ancestral species become separated by a geographical barrier that prevents them from interbreeding, thereby allowing each group to follow its own evolutionary trajectory.
Killer whale populations appear to be going separate evolutionary pathways despite the fact that no known geographical barriers separate them.
Mounting evidence indicates that cultural differences related to food acquisition are driving these populations apart.
The killer whale findings raise questions about diversification within another culture-bearing group of organisms: members of the human family.

PRECEDING PAGES: PAUL NICKLEN Getty Images

become physically separated from each other, often by a geographical barrier of some kind—perhaps a mountain range, desert or river—that prevents the populations from interbreeding. If this separation persists long enough, over time each population will follow its own independent evolutionary trajectory, acquiring different genes that may help them survive in different environmental conditions, for example, or that may accumulate randomly through a process known as genetic drift. Eventually, so the theory goes, the two populations can become so genetically different from each other that if they come into contact again, they cannot interbreed successfully.

Overwhelming evidence from numerous organisms ranging from species of *Alpheus* snapping shrimp that live on either side of the Isthmus of Panama to *Cyprinodon* pupfish species found only in isolated springs in California and Nevada shows that geographical isolation does indeed facilitate the speciation process. Yet sometimes two or more subpopulations of dissimilar appearance will emerge within the same geographical area and ultimately differentiate into separate species. Scientists, including famed German evolutionary biologist Ernst Mayr, traditionally held that at least some period of isolation was essential to the process of speciation and that speciation entirely within the same area was therefore either impossible or at least very rare. More recent work has demonstrated that geographical isolation in the traditional sense is not always necessary for speciation to occur, however.

Indeed, biologists now largely accept that certain species, among them the astonishingly diverse cichlid fishes found in the crater lakes of East Africa and Nicaragua, as well as the *Howea* palm trees found on Lord Howe Island in the Pacific, have evolved in the absence of such isolation. In the parlance of biologists, they have undergone sympatric speciation, and in the case of cichlids, this was apparently mostly driven by different cichlids adapting to exploit different food sources (but without the influence of culture), whereas different Lord Howe palms have evolved different flowering times. Documented examples of sympatric speciation among mammals are rare, though, which makes the case of the killer whales especially interesting.

Killer whales (also called orcas and, in some regions, blackfish) are the most widely distributed mammal on earth after humans. They inhabit all the world's oceans and can travel more than 100 kilometers a day or upward of several thousand kilometers within just a few weeks. There are no known geographical barriers that would prevent individuals from one population from mingling with members of neighboring populations. Yet scientists have now shown that in various marine areas, several ecologically distinct forms, or ecotypes, of killer whales live side by side without fraternizing. One type, for instance, might live mainly on a particular kind of fish, whereas another type might prefer seals.

The best-studied assemblage of killer whale ecotypes lives in the Northeast Pacific. There research begun in the early 1970s by Canadian scientist Michael Bigg led to many remarkable discoveries. First, he noticed that individual killer whales differed in the shape and size of their dorsal fins and in the shape, size and coloration of the so-called saddle patch—the grayish white area behind the dorsal fin. Biologists can use those traits to identify individual killer whales, just as forensic scientists use facial features and fingerprints to identify individual humans. Second, Bigg and his colleagues, including John K. B. Ford and Graeme M. Ellis, both at Fisheries and Oceans Canada, and Kenneth C. Balcomb III of the Center for Whale Research in Washington State, found that three different killer whale ecotypes coexist in the waters off the West Coast of the U.S. and Canada: the so-called resident, transient and offshore forms. Resident killer whales specialize in foraging for fish, especially salmon; transient killer whales target marine mammals and the occasional seabird; and offshore killer whales seem to specialize in a second kind of fish diet that includes Pacific halibut and Pacific sleeper sharks, although their habits remain largely mysterious because encounters with them are rare.

In recent years research led by Olga A. Filatova of Moscow State University, Alexander M. Burdin of the Russian Academy of Sciences, and Erich Hoyt of Whale and Dolphin Conservation in England has revealed that residentlike and transientlike ecotypes also share the Russian waters of the Northwest Pacific around the Kamchatka Peninsula. Thus, we now know that there is a more or less continuous band of resident populations coexisting with transient populations that connect the Northeast Pacific with the Northwest Pacific via the Aleutian Islands.

Halfway across the world, killer whale populations from around Iceland, Shetland and Norway in the Northeast Atlantic have their own food preferences. Scientists, including Volker B. Deecke of the University of Cumbria in England, Andrew D. Foote of the University of Bern in Switzerland and their colleagues, have reported on two groups: type 1 killer whale populations forage for fish, in particular herring and mackerel, and type 2 killer whales pursue seals. More research is needed to fully understand the dietary differences between the groups.

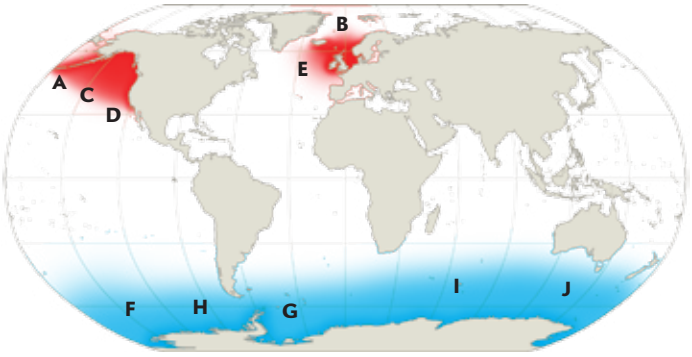
The Southern Hemisphere hosts geographically overlapping ecotypes, too. John W. Durban and Robert L. Pitman, both at the National Oceanic and Atmospheric Administration, and their colleagues have discovered at least four different ones in Antarctic and sub-Antarctic waters. "Type A" killer whales appear to specialize in hunting Antarctic minke whales, "type B" killer whales, on the other hand, come in a large form (the so-called pack ice killer whale) that focuses on seals, and a small form (the Gerlache killer whale) that favors penguins. "Type C"—the smallest known killer whale—hunts Antarctic toothfish. For its part "type D," like the offshore killer whales of the North Pacific, seems to be an open ocean ecotype that remains largely elusive. This ecotype is known to eat Patagonian toothfish from longline fisheries, but it probably dines on other prey as well.

Once scientists realized that all these factions existed within the killer whales, they began to wonder about the origins of these groups. Were the populations already living in the same geographical region when they started to differentiate, or did they start diverging at a time when they lived apart and only later colonized the same region after they had already started down separate evolutionary paths? Current evidence is mostly inconclusive for many Northern Hemisphere killer whales. Whereas several studies by Foote and his colleagues suggest that killer whale divergence in the North Pacific happened while populations were geographically isolated (allopatric speciation), other analyses by Alan Rus Hoelzel of Durham University in England and his collaborators hint that these ecotypes might have always co-existed (sympatric speciation). For the killer whales of the Antarctic, though, the evidence is clearer:

A **Resident**
Preferred prey: fish, especially salmon

Kinds of Killers

Killer whales live in all the world's oceans, without any geographical barriers to keep their populations from interbreeding. Yet studies show that in various regions distinct forms, or ecotypes, have arisen despite living in close proximity to one another. These separate groups, which do not interbreed, differ in their prey choices and how they hunt. They also differ in their physical features, such as body size and coloration, eye patch size, and the shape of the dorsal fin and the saddle patch behind it. The whales choose mates that share their customs rather than foreigners from other ecotypes. Culture appears to keep the ecotypes apart, promoting speciation.



B **Type 1**
Preferred prey: herring and mackerel

F **Type B (Pack Ice)**
Preferred prey: seals

H **Type A**
Preferred prey: Minke whales

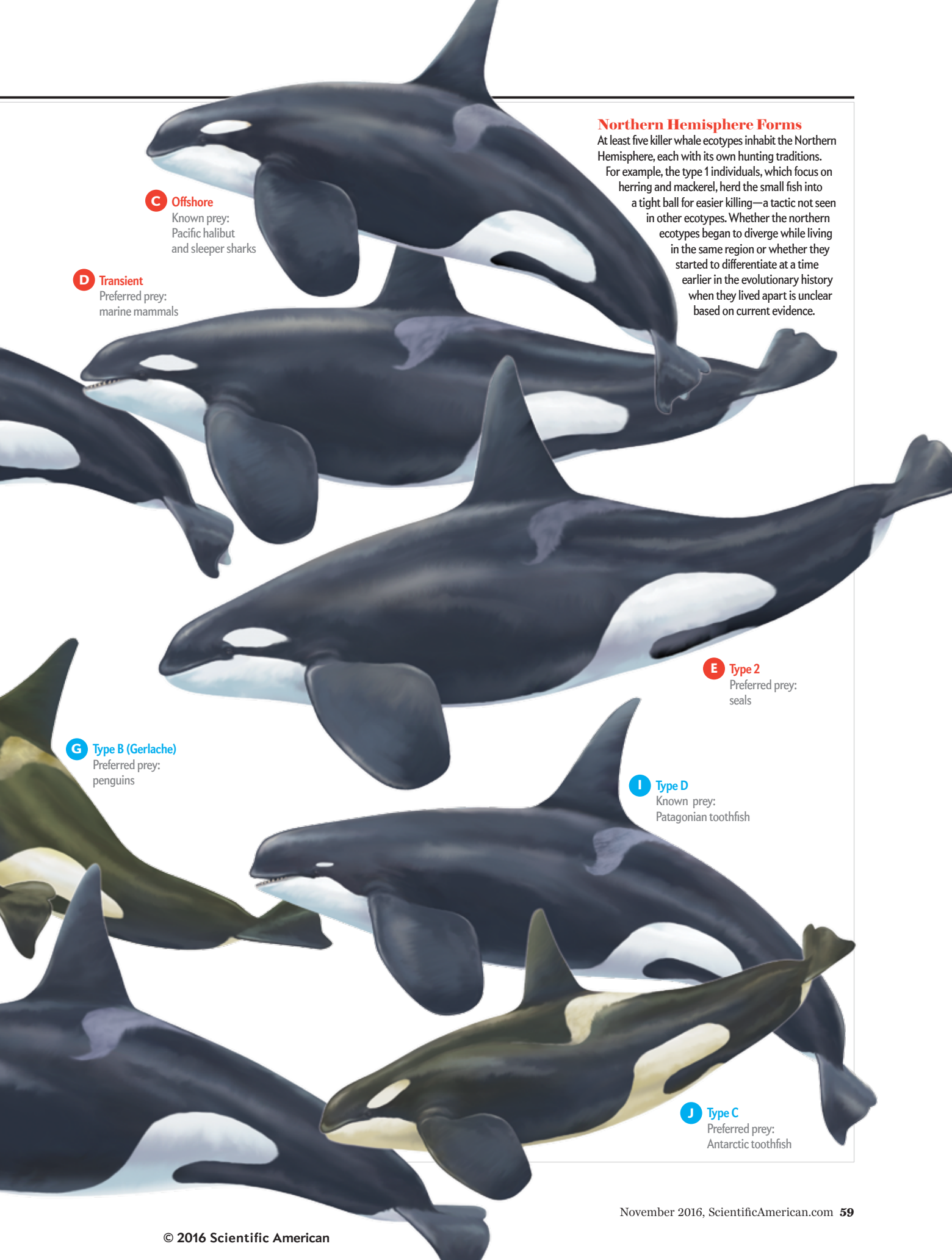
Southern Hemisphere Forms

The Antarctic and sub-Antarctic waters harbor at least five killer whale varieties. Their cultural traditions probably differ depending on their preferred prey. For instance, members of the type B pack ice ecotype have developed a unique strategy called wave washing to push seals off ice floats and into the water, where they are easier to nab. DNA studies indicate that the majority of these forms most likely diverged while living in the same geographical region.

Illustration by Amadeo Bachar

Northern Hemisphere Forms

At least five killer whale ecotypes inhabit the Northern Hemisphere, each with its own hunting traditions. For example, the type 1 individuals, which focus on herring and mackerel, herd the small fish into a tight ball for easier killing—a tactic not seen in other ecotypes. Whether the northern ecotypes began to diverge while living in the same region or whether they started to differentiate at a time earlier in the evolutionary history when they lived apart is unclear based on current evidence.



POD of killer whales surfaces off the coast of British Columbia.

HIROYA MINAKUCHI *National Geographic Creative*

most, if not all, of these killer whale ecotypes probably diverged sympatrically while living in the same geographical region.

However the now sympatric ecotypes initially began to diverge, they did so rapidly. In May of this year, Foote and his colleagues reported that their genomic analysis of five killer whale ecotypes from the North Pacific and the Antarctic showed that these forms evolved from a common ancestor within the past 250,000 years. What is keeping them separate now? Breeding records maintained and occasionally published by SeaWorld, which houses killer whales originally captured in both the North Atlantic and the North Pacific, demonstrate that matings between different killer whale ecotypes produce viable and fertile offspring, in contrast to the usually infertile mules and hinnies that result from hybridization between horses and donkeys. It is therefore extremely unlikely that genetic incompatibilities between killer whale ecotypes are preventing interbreeding in natural populations. Rather mounting evidence suggests that cultural differences are to blame.

CULTURE CLASH

LIKE MANY ORGANISMS that have undergone speciation, killer whales are diversifying by exploiting different food sources and evolving various traits that presumably help them get those foods. Some of these distinguishing features are physical, such as the generally larger, stronger build of the mammal-hunting killer whales. But the most dramatic specializations have occurred in cultural behaviors related to food acquisition. Because these and other behaviors are found only in certain populations where they appear to be passed on between members of the same generation and from generation to generation through social interactions (so-called social learning), rather than being innate, biologists consider them to be cultural.

For example, populations of killer whales that hunt marine mammals have learned to intentionally strand themselves to capture inexperienced sea lion and elephant seal pups right off the beach. Scientists have observed this behavior in two groups of killer whales that are distinct from the previously mentioned ecotypes. One inhabits the waters around the Crozet Archipelago in the Indian Ocean between Africa and Antarctica; the other dwells near the Peninsula Valdés on Argentina's Atlantic Coast. Apparently both populations invented this hunting strategy independently in response to their prey choices and the physical characteristics of their hunting grounds, where deep water channels and river outlets allow the killer whales to stay largely submerged until they are just meters away from their quarry.

In Antarctica, the large, pack ice form of the type B killer whales have invented another ingenious hunting strategy to gain access to seals: wave washing. The seals often haul out on small ice floats, where they feel safe from predators. But the ice-pack killer whales have learned to create waves that wash the seals over the ice float and into the water, where they are easier to nab.

Type 1, fish-eating killer whales around Iceland and Norway, for their part, have developed an entirely different strategy—dubbed carousel feeding—to hunt the herring that form the mainstay of their diet. A pod of the killer whales will herd a school of herring into a tight ball close to the water surface,

SCIENTIFIC AMERICAN ONLINE Learn more about killer whales at ScientificAmerican.com/nov2016/killer-whales

where the fish cannot escape into the depths. Then individual pod members will swim right into the ball and slam their tail fins into the fish to debilitate and kill them.

Killer whales even communicate differently depending on what they eat. Indeed, it is in their acoustic communication signals that the most astonishing cultural diversity is found. Like other dolphins, they use three different acoustic signals: echolocation clicks, which are used to navigate and to locate prey, and pulsed calls and whistles, both of which are used for communication with their compatriots. Not only do the pulsed calls and whistles differ among killer whales from different geographical regions, but they also differ among populations that inhabit the same region.

The reason for this intraregional variation in signal production and use becomes clear when one considers the different challenges the ecotypes face. Killer whales that hunt marine mammals, for example, must contend with the excellent underwater hearing ability of their quarry: eavesdropping prey can use any sound the killer whales produce to detect them and subsequently evade capture. Transient killer whales in the Northeast Pacific and mammal-hunting killer whales in the North Atlantic thus use acoustic signals only very sparingly; most of the time they swim and hunt in stealth mode. Fish-eating killer whales do not have the same problem, so they are typically very chatty with one another, and they do not skimp on echolocation when navigating and tracking prey.

Furthermore, many pulsed calls and, as some of my own research has shown, some whistles are highly stereotyped. That is, the signals can be further differentiated into discrete sounds, like letters in an alphabet. (There is no evidence to suggest that killer whales use these signals in any way that really resembles our human use of words and sentences, however. Rather the context within which a signal is used seems to provide the meaning.) These discrete sounds exhibit geographical variation and ecotype variation. But they also often vary among social groups within an ecotype. For instance, among northern resident killer whales—a population of fish-eating killer whales that inhabits the waters from approximately around the middle of Vancouver Island up into southeastern Alaska—each family unit has its own repertoire of seven to 17 discrete calls. Killer whale families that share a portion of their dialects are grouped together into acoustical clans: A-clan, G-clan and R-clan for the northern resident killer whales.

The different discrete call types and family dialects are so distinctive that those of us who work on these killer whale populations can assign individuals into the correct ecotype, clan (for northern resident killer whales) or even family unit, based on recordings of their discrete call repertoire alone. These differences figure importantly in mate choice. Genetic analyses of the northern residents by Lance Barrett-Lennard of the Vancouver Aquarium Marine Science Center have shown that call similarity largely mirrors genetic similarity. Most matings take place between members of different clans, which have correspondingly different calls. The finding implies that northern residents find other northern residents that sound different from themselves more attractive than those that sound similar. Thus, the dialects offer a nifty way to prevent inbreeding.

That killer whales have all these ecotype-specific customs and appear to dislike socializing and mating with foreigners from other ecotypes despite being biologically capable of doing so suggests that culture is keeping these ecotypes apart. Eventually, if this separation persists for enough generations, then these different ecotypes might evolve additional differences in their DNA that could render them genetically incompatible. Culture in killer whales thus has the potential to take the place of geographical isolation in facilitating speciation by preventing mixing between populations.

The killer whale findings raise interesting questions about diversification within the human family. Traditionally anthropologists thought that most selective pressures that shaped our evolution were the result of changes happening purely in our external environment. But recent genetic analyses indicate that a large part of our evolution might have resulted from certain sometimes very locally restricted, cultural innovations. The practice of cattle farming has driven the evolution of lactose tolerance in certain European and African populations; the high-fat diet of Inuit people in Greenland has driven the evolution of a more efficient fat metabolism in that population. Although all modern human populations clearly belong to the same species and mix routinely with one another, for most of human prehistory, multiple human species shared the planet. Might culture have also played a role in driving speciation among those early members of the human family?

SEPARATE WAYS

DESPITE THE AMAZING ADVANCES in decoding how killer whales have diversified, scientists still have much to learn. Do other areas in less researched regions of the world also host sympatric killer whale ecotypes? Some preliminary studies hint that the oceans around Africa might; those around South America and southern Asia come to mind, too. Also, what are the communications systems of Antarctic and sub-Antarctic killer whales like, and what are their social structures? With the advent of modern tools for studying genomes, the future of speciation research in general—and killer whale research in particular—looks very bright. Perhaps in the not so distant future these and other new technologies will enable us to unequivocally determine what the geographical arrangements of killer whale populations were during all phases of their diversification.

Already we know that culture can divide killer whale populations that live side by side. Maybe a few years from now biologists will recognize these ecotypes as different species, each restricted to a certain geographical area of our oceans, each with its own very specific diet and customs, each with the potential to diverge and form yet more new twigs on the tree of life. SA

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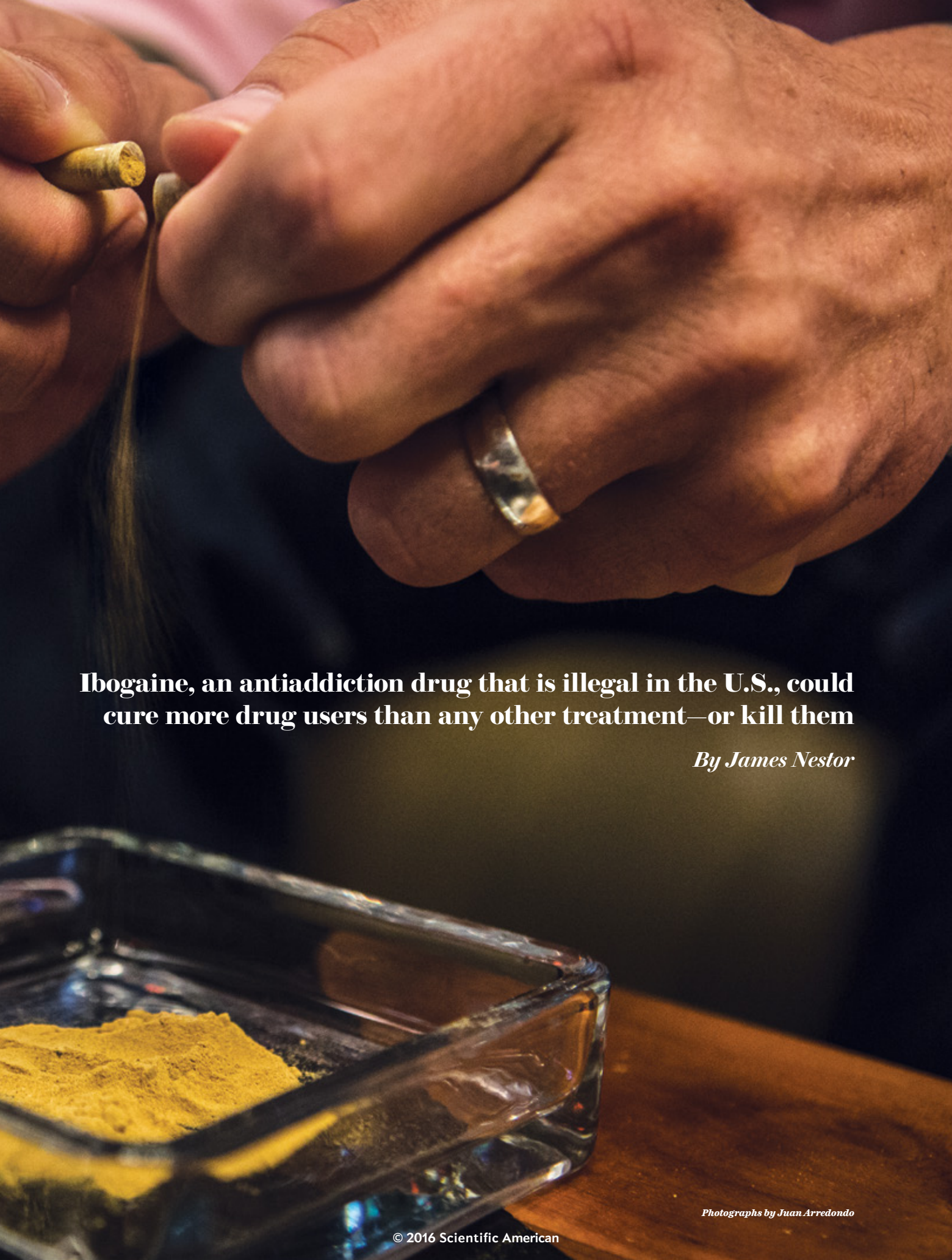
scientificamerican.com/magazine/sa

NEUROSCIENCE

GET CLEAN *or* DIE TRYING

HOPE IN A POWDER: In a clinic in Costa Rica called Envision Recovery, doses of ibogaine powder are prepared for patients. The drug is illegal in the U.S. because of its toxic effects.



Ibogaine, an antiaddiction drug that is illegal in the U.S., could cure more drug users than any other treatment—or kill them

By James Nestor

Photographs by Juan Arredondo

James Nestor is a freelance writer and author of *Deep: Freediving, Renegade Science, and What the Ocean Tells Us about Ourselves* (Houghton Mifflin Harcourt, 2014).

1

A swarm of locusts fills your vision. Thunderclouds cover the bedroom ceiling. Sweats drips from your forehead, chest and hands. You have trouble breathing. The walls around you bend and twist. You cover your eyes, but the scenes play out with the same realer-than-real intensity. An audience somewhere is clapping. The windows of your bedroom disappear into blackness, and 100 stamp-size televisions appear, each one reprising a moment of your childhood: the exact lyrics of a song on the radio you heard once when you were two years old, or the color of your socks at a kindergarten birthday party, or the timbre of your grandfather's voice. This scene bleeds into a darker one of demons, and daggers, and devil armies. You want to get away, but you cannot. You cannot wake up—you cannot move your body. You are Shea Prueger, and you are stuck here for 48 hours.

"It's not the sort of thing anyone would ever want to repeat," Prueger says.

Prueger speaks while swinging in a hanging wicker garden chair at a house in Costa Rica, about 30 miles west of the capital city of San José. The 30-year-old used to live in New York City, work as a model and shoot up heroin. Today she is recalling a desperate attempt five years ago to break her opiate addiction with a psychoactive drug called ibogaine.

She had tried methadone, Suboxone, Narcotics Anonymous and other treatments. Nothing worked. So for two days in 2011 she lay on a mattress in a concrete-walled room in an underground clinic in Guatemala, unable to move, nauseated, while her mind plumbed the deeper recesses of hell. She stayed clean for nine months, relapsed once in June 2012 and says she has not used any narcotics since. "Ibogaine," she insists, "did for me what no other recovery treatment could do."

Recovered addicts, along with a handful of scientists, argue that a dose of ibogaine, a substance derived from a rain-forest shrub called *Tabernanthe iboga,* can "reset" the addiction centers of the brain, freeing people from cravings. As claims have spread, hundreds, perhaps thousands, of people have been flocking to clinics primarily located in Mexico and Central America, where the drug is obtainable—it is illegal in the U.S. In 2006 there were a handful of ibogaine clinics operating worldwide; today, by some estimates, there are around 40. Clinic operators claim that a dose can curb addictive behavior, as well as depression, in about 70 percent of patients.

That success rate, if real, would make ibogaine a sorely needed remedy for an exploding problem. In the U.S., most research indicates that heroin addiction has doubled since 2007, reaching upward of one million addicts today. The increase in needle use has also triggered a new surge in HIV infections. Overall, in

IN BRIEF

Ibogaine, a substance that is derived from a rain-forest shrub, is rumored to free drug addicts from cravings by resetting damaged neural pathways. **Overseas clinics** are luring hundreds of addicts because the drug is illegal in the U.S.; it has been linked to deadly heart problems. **Studies showing** ibogaine is better than methadone are bunk, according to some neuroscientists; others are trying to turn it into a mainstream treatment.

LONG HOURS OF DELIRIUM: Heroin addict Bryan Mallek looks forward to ibogaine treatment at Envision (*1*); after more than a day under ibogaine's hallucinogenic influence, he drags himself up from bed (*2*).

2014 7.1 million Americans had some kind of serious drug problem, according to the National Survey on Drug Use and Health. Many seek help but do so in vain. For example, 40 to 60 percent of treated substance-abuse patients will relapse. About 80 percent do so if they stop taking methadone, the most common opiate replacement therapy.

Ibogaine proponents say it does a better job because it works on many neural pathways at the same time, not just one, as do other treatments. Buoyed by these ideas, two companies, one with partial funding from the National Institute on Drug Abuse (a federal research agency), are currently developing medications based on ibogaine derivatives.

The drug does have a catch: it can kill its users. That is why it is off-limits in the U.S., where the substance has the most restrictive designation possible from the Drug Enforcement Administration. During treatment patients often suffer from cardiac arrhythmia, which can lead to cardiac arrest and sometimes death. Published medical reports tie ibogaine to 19 fatalities in 3,500 treatments between 1990 and 2008. Because informal clinics such as the one in Guatemala may not track all adverse events, the Royal College of Psychiatrists in the U.K. estimates that the fatality rate may be even higher, reaching one in every 300 treatments. Animal studies suggest that the substance, when it does not kill, produces lasting brain damage. "Do we need ibogaine? Not if it there is a toxic part," says Herbert Kleber, a psychiatrist at Columbia University Medical Center.

Yet desperate addicts, failed by methadone, counseling and other treatments, are undeterred by these warnings. Many of them see ibogaine—and all its heart-stopping, brain-degenerating risks—as their last, best chance to get healthy.

A LONG, STRANGE TRIP

IBOGAINE did not make its pharmaceutical debut as an addiction treatment. In small amounts of around eight milligrams, it works as a stimulant. From 1939 to 1970 a French pharmaceutical company mass-produced a tablet form of the drug named Lambarène as a cure for depression, lethargy and infectious diseases. The stimulant properties made ibogaine popular enough among athletes for the International Olympic Committee to ban its use in the 1960s.

Around that time the late Howard Lotsof, then a 19-year-old heroin addict, took some ibogaine for its hallucinogenic effects and told other addicts the drug also reduced his heroin cravings. Word spread, and addicts began using larger doses, up to 20 milligrams per kilogram (mg/kg) of body weight, to help kick their habits. Some animal studies of ibogaine and addiction came out in the late 1980s, and they suggested the substance did curb withdrawal symptoms. The overseas clinics began to open.

Prueger has become evangelical about the substance. After feeling ibogaine's curative powers in 2011, she began administering the drug to other addicts. Prueger is now chief administrator of Envision Recovery, a popular ibogaine clinic in the Costa Rican province of Puntarenas. It is illegal to use ibogaine as medicine in the country—although possession by individuals appears to be allowed—and Envision is not licensed as an addiction treatment center, according to its founder, Lex Kogan. Still, every week Prueger and Kogan host up to half a dozen patients suffering from addictions to alcohol, opiates, amphetamines and prescrip-

tion drugs in an eight-room ranch-style house propped on a steep cliff in a suburban neighborhood, surrounded by lush greenery. Nurses work at the clinic, monitoring patients for adverse effects. Kogan and Prueger do not have formal medical education.

In late December 2014 Bryan Mallek, then a gaunt and frail-looking 29-year-old from West Palm Beach, Fla., showed up asking for help. Mallek has been using heroin for the past 15 years and methadone for about six months. He had tried to get sober dozens of times already. "Nothing else has worked," he told me in a soft and quivering voice. When I interviewed Mallek, he was 10 days into an 18-day program, sitting on a worn leather sofa in the clinic's meeting room. He had been taking small ibogaine doses to test his physical responses for risky reactions, in preparation for a larger dose. An IV line was tied to his right arm, feeding him an electrolyte solution to keep his body hydrated while he fasted on fruit and water. "[Ibogaine] works on the neurochemistry on the brain—that's why I know it will work," he said. "This isn't, you know, talk therapy."

The next day Mallek lay on the sheets of a queen-size bed. He had not taken any opiates for 12 hours and had just entered the first stages of withdrawal—sweats and chills. During the previous two days, a nurse had administered an electrocardiogram to monitor Mallek's heart, especially the rhythms of muscle movements. After a patient ingests ibogaine, his or her heart rate slows, one of the reasons the drug is considered to be so dangerous. Carefully monitoring heart health will help spot arrhythmias in case treatment is needed. After testing, the nurse declared that Mallek's heart and vital signs were healthy. He was ready to begin treatment. Prueger approached with a single gel cap filled with 200 milligrams of ibogaine. Envision purchases the white, powdery substance from a contact in South Africa, Kogan says, who brings it through customs at an airport in Costa Rica in Tupperware containers and has not been stopped. Mallek swallowed the pill, relaxed his head on the pillow, closed his eyes and prepared for two days of hallucinations. "I'm here and ready," he said, his voice quivering. "I want to go now."

Envision has treated more than 1,000 addicts during the past five years, Kogan says. Just like Mallek, these people initially get several small doses to look for problems such as arrhythmias, followed by the high dose intended to produce addiction-curbing effects. Kogan and Prueger have charted patient progress through voluntary phone calls and e-mails over months and even years, and they say that this regimen can cure 75 percent of the people who come to them.

Such claims from clinics sound good but have no solid science behind them, says Luis Eduardo Sandí Esquivel, director of Costa Rica's Institute on Alcoholism and Drug Dependence, the government agency that licenses addiction treatment centers. Clinics that offer ibogaine are simply preying on vulnerable people, he charges: Operators create mystical rituals around the drug and tell addicts "that ibogaine will reset the brain and will take away the addiction. And of course, people pay huge amounts of money for such a beautiful and magical proposal, but this is far from reality." Sandí Esquivel says that he has heard of serious medical complications and relapses connected to ibogaine clinics: "I think [clinics] appeal to the suffering and the pain of human beings and offer magical solutions. It is a manipulation."

There are a few studies by outside researchers that support the notion that ibogaine is therapeutic. In November 2014 research led by neuroscientist Eduardo Schenberg of the Federal University of São Paulo in Brazil looked back at the histories of 75 addicts a year after they took a large dose of ibogaine. (Schenberg reports that he conducted phone interviews and corroborated data with doctors who saw patients during periodic check-ups.) His study, he notes, found that only about 39 percent relapsed into drug use and that those who had a single treatment remained abstinent for 5.5 months on average. That could indicate an improvement over methadone: as noted earlier, 80 percent of methadone patients relapse if they stop taking it. Schenberg's study found addicts who received multiple ibogaine treatments remained off drugs for even longer: a median period of 8.4 months.

1

Medical anthropologist Thomas Kingsley Brown, who has worked with the Multidisciplinary Association for Psychedelic Studies in California, conducted an unpublished study that followed 30 chronic drug users for a year after receiving ibogaine therapy at two clinics in Mexico. Brown says he and his colleagues called patients every month and gave them a questionnaire called the Addiction Severity Index, which measures progress in several problem areas commonly related to addiction, such as psychiatric and social well-being. Two thirds of the patients made it halfway

2

HEART WORRIES: Nurses at Envision check on Mallek (*1*). They worry about abnormal heart rhythms, a potentially deadly side effect of ibogaine, so staffers keep Mallek on a pulse monitor during treatment (*2*).

through the study before dropping out; one third completed all 12 months. The preliminary data showed that all patients benefited from what Brown calls a "huge reduction in withdrawal symptoms." Those who completed the year had significant improvements in social well-being. The study did not follow them further, so Brown does not know how many, if any, relapsed into drug use.

Despite Mallek's disparaging remark about "talk therapy," Brown thinks ibogaine cannot work well without it. Counseling helps patients identify addiction causes such as emotional trauma or physical pain, and ibogaine, he says, interrupts physical cravings and stems withdrawal symptoms. This double effect can, according to Brown, "greatly strengthen people's resolve to live sober, honest lives again."

DEATH AND DAMAGE

NO ADDICTS will lead a decent life, of course, if ibogaine kills them. The heart risks have been well documented. There is also the potential of harm to the brain. In the 1990s several animal studies at Johns Hopkins University showed severe brain lesions and degeneration of cerebellar Purkinje cells, large neurons that control aspects of motor function, in rats given doses of about 100 mg/kg of ibogaine (equivalent to a human dose of about 16 mg/kg). Further, in 1996 an Environmental Protection Agency study showed, in rats given 100 mg/kg of the drug, an enormous increase in glial fibrillary acidic protein (GFAP), which can weaken the structure of brain and spinal cord cells, in certain parts of the brain: up to 215 percent in the brain stem and up to 142 percent in the striatum. (There was no observed effect on the cerebellum.)

The extent of damage in Purkinje cells and the potential for damage from GFAP spikes seem tied to dosage. When researchers at Albany Medical College administered doses of 40 mg/kg of ibogaine to opioid-addicted rats (about 6.5 mg/kg in average-sized humans; Mallek's large dose was about 8 mg/kg), there was no observable Purkinje cell degeneration. In a University of Arkansas and National Center for Toxicological Research study, some rats were dosed at smaller 25 mg/kg levels more than a dozen times over a month with no observed evidence of neurotoxicity.

In people, smaller doses (as little as 4.5 mg/kg) have proved to be fatal to one confirmed patient. Ibogaine's restrictive Schedule I status and lack of funding sources have made it nearly impossible for researchers to run clinical toxicology studies on humans to learn why.

In 1993 Deborah Mash, a neuropharmacologist at the University of Miami's school of medicine, did get U.S. Food and Drug Administration approval to begin a safety study of ibogaine in cocaine-dependent volunteers. The initial results were positive: the beginning dose of 1 and 2 mg/kg hurt no one. But when Mash sought funding from NIDA to conduct research on higher doses and to begin a larger study, which included investigating safety—measuring the time it took patients to metabolize the drug and determining whether any genes in the patients affected those outcomes—NIDA refused, claiming that ibogaine was simply too unpredictable for human trials.

"It's a pharmacologist's nightmare," says Frank Vocci, former chief of drug abuse research at the FDA, who oversaw ibogaine studies at NIDA in the 1990s. One of the primary issues with the drug, Vocci argues, is that it was very hard for researchers to gauge a predictable dose across a population. "We surveyed the [existing] studies and found something like two deaths for 100 people who had taken ibogaine," Vocci says. "You can't run a program with those kinds of risks. The safety data are just so bad."

Mash, however, thought her early results meant she was onto something, despite NIDA's misgivings. With funding from private investors and patients themselves, she continued drug metabolism, safety and efficacy research on more than 300 chronic users at a clinic on the Caribbean island of Saint Kitts between 1996 and 2004. Using follow-up data on patients after treatment, Mash reported that ibogaine detox blocked at least 90 percent of the opiate withdrawal symptoms in chronic heroin users. More than half of the patients stayed clean a year after the treatment, according to self-reports and family interviews.

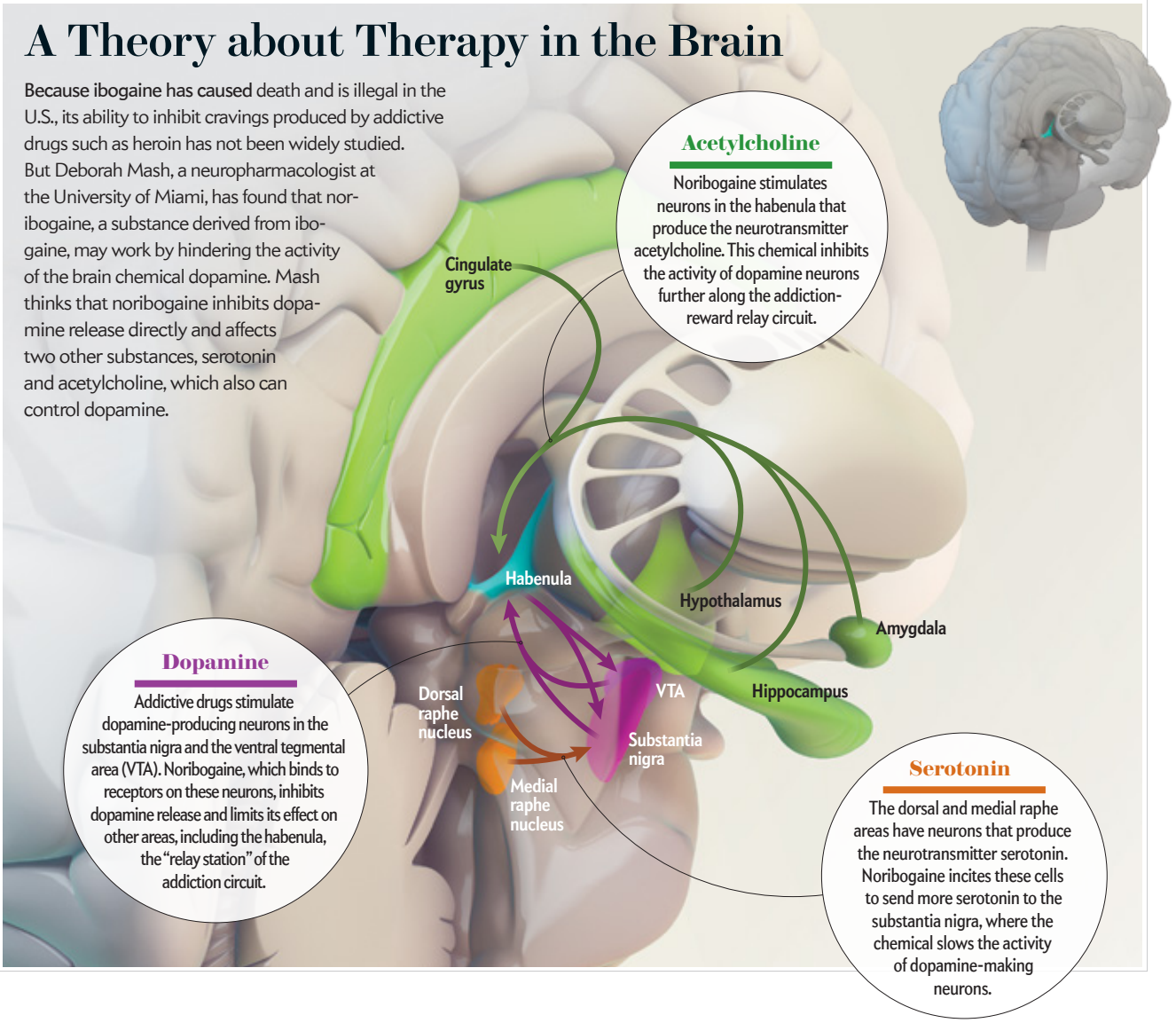
Mash used this work to develop a theory about how ibogaine works in the brain and what—she believes—makes the drug so powerful. From a molecular perspective, all life's euphoric moments—joy, gratification and arousal—are the result of dopamine, serotonin and other chemicals, called neurotransmitters, signaling across billions of nerve cells in the reward centers of the brain. The more of these neurotransmitters that are active in the brain's reward areas, the better we feel. When a strong opioid such as heroin is introduced into the body, it triggers a release of dopamine and other neurotransmitters into these reward centers, creating the drug's "high." If a person continues taking heroin, the brain will become accustomed to the constant presence of the drug, and the neural networks in the reward centers will adapt. If a person stops, the body and brain begin to crave the chemicals that are no longer there—and the results are withdrawal cravings.

Ibogaine works, Mash says, because it does not simply substitute for heroin on one of these neural pathways, as, say, methadone does. In the body, ibogaine breaks down to noribogaine, which affects several paths—including the dopamine system, along with circuits involving neurotransmitters such as serotonin and acetylcholine—that interact to pass along or block craving signals [*see box on next page*].

But without money for research, Mash has not been able to

A Theory about Therapy in the Brain

Because ibogaine has caused death and is illegal in the U.S., its ability to inhibit cravings produced by addictive drugs such as heroin has not been widely studied. But Deborah Mash, a neuropharmacologist at the University of Miami, has found that noribogaine, a substance derived from ibogaine, may work by hindering the activity of the brain chemical dopamine. Mash thinks that noribogaine inhibits dopamine release directly and affects two other substances, serotonin and acetylcholine, which also can control dopamine.



verify or elaborate on this preliminary work. "The bottom line is without funding from the National Institutes of Health or a pharma sponsor, you don't go forward," she says.

DETOX THE DRUG

FOR STANLEY GLICK, ibogaine's costs and benefits would balance much more easily with fewer side effects. Glick, professor emeritus in the department of neuroscience and experimental therapeutics at Albany Medical Center, first heard about the drug's potential and its dangers in the 1990s. He and chemist Martin E. Kuehne began trying to distill the active agents out of ibogaine while leaving all its toxic components behind. In 1996 Glick and Kuehne developed a synthetic analogue of ibogaine named 18-methoxycoronaridine, or 18-MC. Research in the 1990s with laboratory animals showed that 18-MC effectively blocked alpha-3 beta-4 nicotinic receptors in the brain, which are believed to play a significant role in addiction, without affecting the serotonergic system. Researchers believe the serotonergic system is largely responsible for ibogaine's hallucinations. "It puts a chilling effect on anything that raises the level of dopamine too high," Glick says—everything from heroin to alcohol to food.

For the past decade Glick has led several studies on both ibogaine and 18-MC's efficacy in curbing addictions in rodents and humans. After a couple of unsuccessful earlier attempts to bring 18-MC to market, he partnered with Savant HWP, a privately held drug-development company in northern California, in 2009. In September 2014 Savant HWP received more than $6.5 million from NIDA to conduct human trials of 18-MC. Results of an unpublished double-blind, placebo-controlled study conducted by Savant HWP's partner company in Brazil in 2014 showed all volunteers given therapeutic dosages of 18-MC suffered no adverse effects of the drug—hallucinations, cardiac reaction, Purkinje cell damage or any other neurotoxicity. Savant HWP plans to run clinical trials of 18-MC in 2017, first with smokers in Brazil, followed by tests with opioid and cocaine addicts in the U.S.

Mash is not far behind. Inspired by the results of her eight years of ibogaine trials on Saint Kitts, Mash helped to found DemeRx, a private drug-development research company work-

SOURCES: DEBORAH MASH: "THE ROLE OF THE HABENULA IN DRUG ADDICTION," BY KENIA M. VELASQUEZ ET AL., IN *FRONTIERS IN HUMAN NEUROSCIENCE*, VOL. 8, ARTICLE NO. 174; MARCH 28, 2014

SCIENTIFIC AMERICAN ONLINE Read about standard opioid addiction treatments at ScientificAmerican.com/nov2016/detox

Illustration by AXS Biomedical Animation Studio

BELIEVERS: Shea Prueger (*left*) and Lex Kogan (*right*) run Envision. Both think that ibogaine cures not only drug addiction but depression; they treat patients for both problems.

ing to bring noribogaine, another ibogaine-derived drug, to market. In February 2015 a New Zealand team of scientists, building on the company's research, published a safety study of noribogaine on 36 healthy drug-free male volunteers. The volunteers received various therapeutic oral doses of noribogaine or a matching placebo and were then monitored over the course of 216 hours. The scientists said there were no adverse effects from either the placebo or noribogaine. Early research suggests that noribogaine, like 18-MC, may also share ibogaine's ability to stem withdrawals and curb addictions but without the side effects.

Unpublished DemeRx preclinical toxicology studies have so far demonstrated that noribogaine with two-week chronic exposures does not cause some of the neurologicial problems noted by other studies: cerebellar Purkinje cell degeneration or GFAP activation. The company has filed an Investigational New Drug application in the U.S. for noribogaine, and proof-of-concept studies for the drug are currently under way.

The patient pool that drives Glick and Mash forward is made up of not just drug addicts but people with a much more common disease: depression. Today one in 10 Americans takes an antidepressant medication; among women in their 40s and 50s, that figure increases to one in four. Mood-enhancing pharmaceutical drugs such as fluoxetine, more commonly known by its trade name Prozac, work as selective serotonin reuptake inhibitors (SSRIs), blocking the reabsorption of serotonin by a neuron. Serotonin is a neurotransmitter that plays a role in sending messages in the brain; an increase in serotonin results in increased brain activity, which appears to boost the mood of patients with depression. But Prozac and other SSRIs are not always effective. According to a 2010 study in the *Journal of the American Medical Association,* placebos had the same effect as SSRIs in most people suffering from moderate or mild depression. A National Institute of Mental Health–funded study from 2006 found that about 70 percent of people who took SSRIs experienced the same depressive symptoms after 14 weeks. A number of depressed patients, failed by these drugs, turn to ibogaine to normalize their presumed chemical imbalance.

Kogan says that about 80 percent of patients suffering from depression who come to Envision Recovery will permanently cease taking SSRIs and leave happy and healthy after treatment. Although there is no established scientific support for this claim, Kogan says his clinic has seen a 300 percent increase in SSRI users from just three years ago; these patients now constitute 30 percent of all Envision customers. Kogan predicts those numbers will double in the coming years. And Glick thinks that a nontoxic ibogaine analogue will be an important addition to the antidepressant arsenal.

DEMAND AND SUPPLY

AT ENVISION, four days after Mallek received his big ibogaine dose, he was rushing to pack his bags before taking a bus to Costa Rica's western coast for a sightseeing tour. "I'm going to go see some monkeys, sit on a beach, whatever!" he said. His face was flush, and he was chatty and energetic. "I have no cravings, no withdrawals," Mallek said, flashing a smile. "People try to quit so many different ways, and they all fail. But this works for everybody. This stuff's a miracle."

Mallek is wrong. In fact, ibogaine does not work for everybody. It did not even work for Mallek this time. He was clean for four months, and then he relapsed. Patients like him, and the concerns about harm caused by the drug, are reasons that—until there are placebo-controlled, randomized, double-blinded clinical trials in multiple centers—ibogaine will remain an outlier of addiction therapy, relegated to unregulated clinics. And none of this rigorous research is on the horizon, because safety concerns make it unlikely that government institutions in the U.S. or Europe will allocate funds for it. Private pharmaceutical companies have shown little interest in the drug because of this same danger and because it is not easily patentable.

Still, the large number of addicts looking to cleanse their demons means that ibogaine is not going to disappear anytime soon. Mallek, for instance, did not blame the drug for his relapse but instead faulted his own weakness. "I don't want to say that ibogaine gives people their lives back, more so that it gives people the *ability* to take their lives back," he wrote to me in an e-mail. "But freedom without wisdom can be a dangerous thing." Mallek also thought he had acquired some wisdom, at least about his personal flaws. He was planning a return trip to Envision for a follow-up treatment. He was determined to get clean, no matter the risks. SA

MORE TO EXPLORE

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LINGUISTICS

LANGUAGE IN A NEW KEY

Much of Noam Chomsky's revolution in linguistics—including its account of the way we learn languages—is being overturned

By Paul Ibbotson and Michael Tomasello

THE IDEA THAT WE HAVE BRAINS HARDWIRED WITH A MENTAL TEMPLATE FOR LEARNING GRAMMAR—famously espoused by Noam Chomsky of the Massachusetts Institute of Technology—has dominated linguistics for almost half a century. Recently, though, cognitive scientists and linguists have abandoned Chomsky's "universal grammar" theory in droves because of new research examining many different languages—and the way young children learn to understand and speak the tongues of their communities. That work fails to support Chomsky's assertions.

The research suggests a radically different view, in which learning of a child's first language does not rely on an innate grammar module. Instead the new research shows that young children use various types of thinking that may not be specific to language at all—such as the ability to classify the world into categories (people or objects, for instance) and to understand the relations

IN BRIEF

Noam Chomsky has been a towering giant in the field of linguistics for many decades, famed for his well-known theory of universal grammar.

Chomsky's idea of a brain wired with a mental template for grammar has been questioned, based on a lack of evidence from field studies of languages.

The theory has changed several times to account for exceptions that run counter to its original postulations—marking a retreat from its ambitious origins.

Alternatives to universal grammar posit that children learning language use general cognitive abilities and the reading of other people's intentions.

Illustration by Owen Gildersleeve

among things. These capabilities, coupled with a unique human ability to grasp what others intend to communicate, allow language to happen. The new findings indicate that if researchers truly want to understand how children, and others, learn languages, they need to look outside of Chomsky's theory for guidance.

This conclusion is important because the study of language plays a central role in diverse disciplines—from poetry to artificial intelligence to linguistics itself; misguided methods lead to questionable results. Further, language is used by humans in ways no animal can match; if you understand what language *is,* you comprehend a little bit more about human nature.

Chomsky's first version of his theory, put forward in the mid-20th century, meshed with two emerging trends in Western intellectual life. First, he posited that the languages people use to communicate in everyday life behaved like mathematically based languages of the newly emerging field of computer science. His research looked for the underlying computational structure of language and proposed a set of procedures that would create "well-formed" sentences. The revolutionary idea was that a computerlike program could produce sentences real people thought were grammatical. That program could also purportedly explain the way people generated their sentences. This way of talking about language resonated with many scholars eager to embrace a computational approach to … well … everything.

As Chomsky was developing his computational theories, he was simultaneously proposing that they were rooted in human biology. In the second half of the 20th century, it was becoming ever clearer that our unique evolutionary history was responsible for many aspects of our unique human psychology, and so the theory resonated on that level as well. His universal grammar was put forward as an innate component of the human mind—and it promised to reveal the deep biological underpinnings of the world's 6,000-plus human languages. The most powerful, not to mention the most beautiful, theories in science reveal hidden unity underneath surface diversity, and so this theory held immediate appeal.

But evidence has overtaken Chomsky's theory, which has been inching toward a slow death for years. It is dying so slowly because, as physicist Max Planck once noted, older scholars tend to hang on to the old ways: "Science progresses one funeral at a time."

IN THE BEGINNING

THE EARLIEST INCARNATIONS of universal grammar in the 1960s took the underlying structure of "standard average European" languages as their starting point—the ones spoken by most of the linguists working on them. Thus, the universal grammar program operated on chunks of language, such as noun phrases ("The nice dogs") and verb phrases ("like cats").

Fairly soon, however, linguistic comparisons among multiple languages began rolling in that did not fit with this neat schema. Some native Australian languages, such as Warlpiri, had grammatical elements scattered all over the sentence—noun and verb phrases that were not "neatly packaged" so that they could be plugged into Chomsky's universal grammar—and some sentences had no verb phrase at all.

These so-called outliers were difficult to reconcile with the universal grammar that was built on examples from European languages. Other exceptions to Chomsky's theory came from the study of "ergative" languages, such as Basque or Urdu, in which the way a sentence subject is used is very different from that in many European languages, again challenging the idea of a universal grammar.

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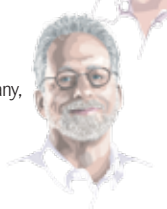
Michael Tomasello is co-director of the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany, and author, most recently, of *A Natural History of Human Morality* (Harvard University Press, 2016).



These findings, along with theoretical linguistic work, led Chomsky and his followers to a wholesale revision of the notion of universal grammar during the 1980s. The new version of the theory, called principles and parameters, replaced a single universal grammar for all the world's languages with a set of "universal" principles governing the structure of language. These principles manifested themselves differently in each language. An analogy might be that we are all born with a basic set of tastes (sweet, sour, bitter, salty and umami) that interact with culture, history and geography to produce the present-day variations in world cuisine. The principles and parameters were a linguistic analogy to tastes. They interacted with culture (whether a child was learning Japanese or English) to produce today's variation in languages as well as defined the set of human languages that were possible.

Languages such as Spanish form fully grammatical sentences without the need for separate subjects—for example, *Tengo zapatos* ("I have shoes"), in which the person who has the shoes, "I," is indicated not by a separate word but by the "o" at the end of the verb. Chomsky contended that as soon as children encountered a few sentences of this type, their brains would set a switch to "on," indicating that the sentence subject should be dropped. Then they would know that they could drop the subject in all their sentences.

The "subject-drop" parameter supposedly also determined other structural features of the language. This notion of universal principles fits many European languages reasonably well. But data from non-European languages turned out not to fit the revised version of Chomsky's theory. Indeed, the research that had attempted to identify parameters, such as the subject-drop, ultimately led to the abandonment of the second incarnation of universal grammar because of its failure to stand up to scrutiny.

More recently, in a famous paper published in *Science* in 2002, Chomsky and his co-authors described a universal grammar that included only one feature, called computational recursion (although many advocates of universal grammar still prefer to assume there are many universal principles and parameters). This new shift permitted a limited number of words and rules to be combined to make an unlimited number of sentences.

The endless possibilities exist because of the way recursion embeds a phrase *within* another phrase of the same type. For example, English can embed phrases to the right ("John hopes Mary knows Peter is lying") or embed centrally ("The dog that the cat that the boy saw chased barked"). In theory, it is possible to go

on embedding these phases infinitely. In practice, understanding starts to break down when the phrases are stacked on top of one another as in these examples. Chomsky thought this breakdown was not directly related to language per se. Rather it was a limitation of human memory. More important, Chomsky proposed that this recursive ability is what sets language apart from other types of thinking such as categorization and perceiving the relations among things. He also proposed recently this ability arose from a single genetic mutation that occurred between 100,000 and 50,000 years ago.

As before, when linguists actually went looking at the variation in languages across the world, they found counterexamples to the claim that this type of recursion was an essential property of language. Some languages—the Amazonian Pirahã, for instance—seem to get by without Chomskyan recursion.

As with all linguistic theories, Chomsky's universal grammar tries to perform a balancing act. The theory has to be simple enough to be worth having. That is, it must predict some things that are not in the theory itself (otherwise it is just a list of facts). But neither can the theory be so simple that it cannot explain things it should. Take Chomsky's idea that sentences in all the world's languages have a "subject." The problem is the concept of a subject is more like a "family resemblance" of features than a neat category. About 30 different grammatical features define the characteristics of a subject. Any one language will have only a subset of these features—and the subsets often do not overlap with those of other languages.

The brain's innate sentence-diagramming machine, according to Chomsky, would fit words into correct grammatical slots—"nice" (adjective), "dogs" (noun).

Chomsky tried to define the components of the essential tool kit of language—the kinds of mental machinery that allow human language to happen. Where counterexamples have been found, some Chomsky defenders have responded that just because a language lacks a certain tool—recursion, for example—does not mean that it is not in the tool kit. In the same way, just because a culture lacks salt to season food does not mean salty is not in its basic taste repertoire. Unfortunately, this line of reasoning makes Chomsky's proposals difficult to test in practice, and in places they verge on the unfalsifiable.

DEATH KNELLS

A KEY FLAW in Chomsky's theories is that when applied to language learning, they stipulate that young children come equipped with the capacity to form sentences using abstract grammatical rules. (The precise ones depend on which version of the theory is invoked.) Yet much research now shows that language acquisition does not take place this way. Rather young children begin by learning simple grammatical patterns; then, gradually, they intuit the rules behind them bit by bit.

Thus, young children initially speak with only concrete and simple grammatical constructions based on specific patterns of words: "Where's the X?"; "I wanna X"; "More X"; "It's an X"; "I'm X-ing it"; "Put X here"; "Mommy's X-ing it"; "Let's X it"; "Throw X"; "X gone"; "Mommy X"; "I Xed it"; "Sit on the X"; "Open X"; "X here"; "There's an X"; "X broken." Later, children combine these early patterns into more complex ones, such as "Where's the X that Mommy Xed?"

Many proponents of universal grammar accept this characterization of children's early grammatical development. But then

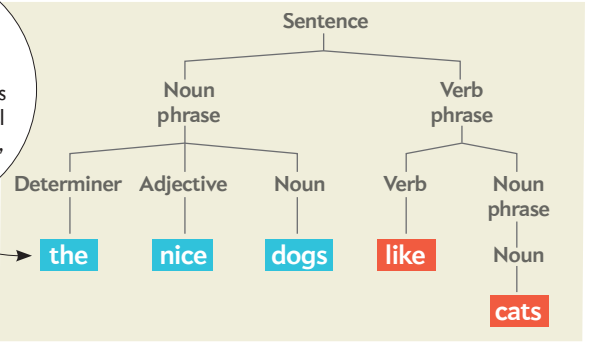
THEORIES OF LANGUAGE

Noam-enclature

Noam Chomsky took the linguistics community by storm more than 50 years ago. The idea was simple. Underlying language is a set of rules innate to every child that generates grammatical sentences from the earliest age. Chomsky set out to define those rules and how they work. Without this universal grammar, he thought, it would be impossible for a child to learn any language. In the ensuing years, Chomsky's theory has gradually been challenged by new theories asserting that language is acquired as children discern patterns in the language they hear around them.

Chomsky's Universal Grammar

Chomsky's universal grammar equipped the child with rules that worked on phrases ("the nice dogs") and rules for transforming those phrases ("Cats are liked by the nice dogs"). The theory has evolved in recent years but still retains the essential idea that children are born with the ability to make words conform to a grammatical template.



Usage-Based Learning

New approaches to linguistics and psychology suggest that children's natural ability to intuit what others think, combined with powerful learning mechanisms in the developing brain, diminishes the need for a universal grammar. Through listening, the child learns patterns of usage that can be applied to different sentences. The word "food" might replace the word "ball" after the phrase "The dog wants." Studies show that this theory of building up knowledge of word meaning and grammar approximates the way that two- and three-year-olds actually learn language.

Illustration by Lucy Reading-Ikkanda

they assume that when more complex constructions emerge, this new stage reflects the maturing of a cognitive capacity that uses universal grammar and its abstract grammatical categories and principles.

For example, most universal grammar approaches postulate that a child forms a question by following a set of rules based on grammatical categories such as "What (object) did (auxiliary) you (subject) lose (verb)?" Answer: "I (subject) lost (verb) something (object)." If this postulate is correct, then at a given developmental period children should make similar errors across all wh-question sentences alike. But children's errors do not fit this prediction. Many of them early in development make errors such as "Why he can't come?" but at the same time as they make this error—failing to put the "can't" before the "he"—they correctly form other questions with other "wh-words" and auxiliary verbs, such as the sentence "What does he want?"

Experimental studies confirm that children produce correct question sentences most often with particular wh-words and auxiliary verbs (often those with which they have most experience, such as "What does …"), while continuing to make errors with question sentences containing other (often less frequent) combinations of wh-words and auxiliary verbs: "Why he can't come?"

In the new usage-based approach, children are not born with a universal, dedicated tool for the learning of grammar. Instead they inherit the mental equivalent of a Swiss Army knife.

The main response of universal grammarians to such findings is that children have the competence with grammar but that other factors can impede their performance and thus both hide the true nature of their grammar and get in the way of studying the "pure" grammar posited by Chomsky's linguistics. Among the factors that mask the underlying grammar, they say, include immature memory, attention and social capacities.

Yet the Chomskyan interpretation of the children's behavior is not the only possibility. Memory, attention and social abilities may not mask the true status of grammar; rather they may well be integral to building a language in the first place. For example, a recent study co-authored by one of us (Ibbotson) showed that children's ability to produce a correct irregular past tense verb—such as "Every day I fly, yesterday I *flew*" (not "flyed")—was associated with their ability to inhibit a tempting response that was unrelated to grammar. (For example, to say the word "moon" while looking at a picture of the sun.) Rather than memory, mental analogies, attention and reasoning about social situations getting in the way of children expressing the pure grammar of Chomskyan linguistics, those mental faculties may explain why language develops as it does.

As with the retreat from the cross-linguistic data and the tool-kit argument, the idea of performance masking competence is also pretty much unfalsifiable. Retreats to this type of claim are common in declining scientific paradigms that lack a strong empirical base—consider, for instance, Freudian psychology and Marxist interpretations of history.

Even beyond these empirical challenges to universal grammar, psycholinguists who work with children have difficulty conceiving theoretically of a process in which children start with the same algebraic grammatical rules for all languages and then proceed to figure out how a particular language—whether English or Swahili—connects with that rule scheme. Linguists call this conundrum the linking problem, and a rare systematic attempt to solve it in the context of universal grammar was made by Harvard University psychologist Steven Pinker for sentence subjects. Pinker's account, however, turned out not to agree with data from child development studies or to be applicable to grammatical categories other than subjects. And so the linking problem—which should be the central problem in applying universal grammar to language learning—has never been solved or even seriously confronted.

AN ALTERNATIVE VIEW

ALL OF THIS LEADS ineluctably to the view that the notion of universal grammar is plain wrong. Of course, scientists never give up on their favorite theory, even in the face of contradictory evidence, until a reasonable alternative appears. Such an alternative, called usage-based linguistics, has now arrived. The theory, which takes a number of forms, proposes that grammatical structure is not innate. Instead grammar is the product of history (the processes that shape how languages are passed from one generation to the next) and human psychology (the set of social and cognitive capacities that allow generations to learn a language in the first place). More important, this theory proposes that language recruits brain systems that may not have evolved specifically for that purpose and so is a different idea to Chomsky's single-gene mutation for recursion.

In the new usage-based approach (which includes ideas from functional linguistics, cognitive linguistics and construction grammar), children are not born with a universal, dedicated tool for learning grammar. Instead they inherit the mental equivalent of a Swiss Army knife: a set of general-purpose tools—such as categorization, the reading of communicative intentions, and analogy making, with which children build grammatical categories and rules from the language they hear around them.

For instance, English-speaking children understand "The cat ate the rabbit," and by analogy they also understand "The goat tickled the fairy." They generalize from hearing one example to another. After enough examples of this kind, they might even be able to guess who did what to whom in the sentence "The gazzer mibbed the toma," even though some of the words are literally nonsensical. The grammar must be something they discern beyond the words themselves, given that the sentences share little in common at the word level.

The meaning in language emerges through an interaction between the potential meaning of the words themselves (such as the things that the word "ate" can mean) and the meaning of the grammatical construction into which they are plugged. For example, even though "sneeze" is in the dictionary as an intransitive verb that only goes with a single actor (the one who sneezes), if one forces it into a ditransitive construction—one able to

SCIENTIFIC AMERICAN ONLINE Watch Tomasello give a talk on human communication at ScientificAmerican.com/nov2016/tomasello

take both a direct and indirect object—the result might be "She sneezed him the napkin," in which "sneeze" is construed as an action of transfer (that is to say, she made the napkin go to him). The sentence shows that grammatical structure can make as strong a contribution to the meaning of the utterance as do the words. Contrast this idea with that of Chomsky, who argued there are levels of grammar that are free of meaning entirely.

The concept of the Swiss Army knife also explains language learning without any need to invoke two phenomena required by the universal grammar theory. One is a series of algebraic rules for combining symbols—a so-called core grammar hardwired in the brain. The second is a lexicon—a list of exceptions that cover all of the other idioms and idiosyncrasies of natural languages that must be learned. The problem with this dual-route approach is that some grammatical constructions are partially rule-based and also partially not—for example, "Him a presidential candidate?!" in which the subject "him" retains the form of a direct object but with the elements of the sentence not in the proper order. A native English speaker can generate an infinite variety of sentences using the same approach: "Her go to ballet?!" or "That guy a doctor?!" So the question becomes, are these utterances part of the core grammar or the list of exceptions? If they are not part of a core grammar, then they must be learned individually as separate items. But if children can learn these part-rule, part-exception utterances, then why can they not learn the rest of language the same way? In other words, why do they need universal grammar at all?

In fact, the idea of universal grammar contradicts evidence showing that children learn language through social interaction and gain practice using sentence constructions that have been created by linguistic communities over time. In some cases, we have good data on exactly how such learning happens. For example, relative clauses are quite common in the world's languages and often derive from a meshing of separate sentences. Thus, we might say, "My brother.... He lives over in Arkansas.... He likes to play piano." Because of various cognitive-processing mechanisms—with names such as schematization, habituation, decontextualization and automatization—these phrases evolve over long periods into a more complex construction: "My brother, who lives over in Arkansas, likes to play the piano." Or they might turn sentences such as "I pulled the door, and it shut" gradually into "I pulled the door shut."

What is more, we seem to have a species-specific ability to decode others' communicative intentions—what a speaker intends to say. For example, I could say, "She gave/bequeathed/sent/loaned/sold the library some books" but not "She donated the library some books." Recent research has shown that there are several mechanisms that lead children to constrain these types of inappropriate analogies. For example, children do not make analogies that make no sense. So they would never be tempted to say "She ate the library some books." In addition, if children hear quite often "She donated some books to the library," then this usage preempts the temptation to say "She donated the library some books."

Such constraining mechanisms vastly cut down the possible analogies a child could make to those that align the communicative intentions of the person he or she is trying to understand. We all use this kind of intention reading when we understand "Can you open the door for me?" as a request for help rather than an inquiry into door-opening abilities.

Chomsky allowed for this kind of "pragmatics"—how we use language in context—in his general theory of how language worked. Given how ambiguous language is, he had to. But he appeared to treat the role of pragmatics as peripheral to the main job of grammar. In a way, the contributions from usage-based approaches have shifted the debate in the other direction to how much pragmatics can do for language before speakers need to turn to the rules of syntax.

Usage-based theories are far from offering a complete account of how language works. Meaningful generalizations that children make from hearing spoken sentences and phrases are not the whole story of how children construct sentences either—there are generalizations that make sense but are not grammatical (for example, "He disappeared the rabbit"). Out of all the possible meaningful yet ungrammatical generalizations children could make, they appear to make very few. The reason seems to be they are sensitive to the fact that the language community to which they belong conforms to a norm and communicates an idea in just "this way." They strike a delicate balance, though, as the language of children is both creative ("I goed to the shops") and conformative to grammatical norms ("I went to the shops"). There is much work to be done by usage-based theorists to explain how these forces interact in childhood in a way that exactly explains the path of language development.

A LOOK AHEAD

AT THE TIME the Chomskyan paradigm was proposed, it was a radical break from the more informal approaches prevalent at the time, and it drew attention to all the cognitive complexities involved in becoming competent at speaking and understanding language. But at the same time that theories such as Chomsky's allowed us to see new things, they also blinded us to other aspects of language. In linguistics and allied fields, many researchers are becoming ever more dissatisfied with a totally formal language approach such as universal grammar—not to mention the empirical inadequacies of the theory. Moreover, many modern researchers are also unhappy with armchair theoretical analyses, when there are large corpora of linguistic data—many now available online—that can be analyzed to test a theory.

The paradigm shift is certainly not complete, but to many it seems that a breath of fresh air has entered the field of linguistics. There are exciting new discoveries to be made by investigating the details of the world's different languages, how they are similar to and different from one another, how they change historically, and how young children acquire competence in one or more of them.

Universal grammar appears to have reached a final impasse. In its place, research on usage-based linguistics can provide a path forward for empirical studies of learning, use and historical development of the world's 6,000 languages. SA

MORE TO EXPLORE

Constructing a Language: A Usage-Based Theory of Language Acquisition. Michael Tomasello. Harvard University Press, 2003.

Constructions at Work: The Nature of Generalization in Language. Adele Goldberg. Oxford University Press, 2006.

Language, Usage and Cognition. Joan Bybee. Cambridge University Press, 2010.

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The "It" Factor. Gary Stix; September 2014.

scientificamerican.com/magazine/sa

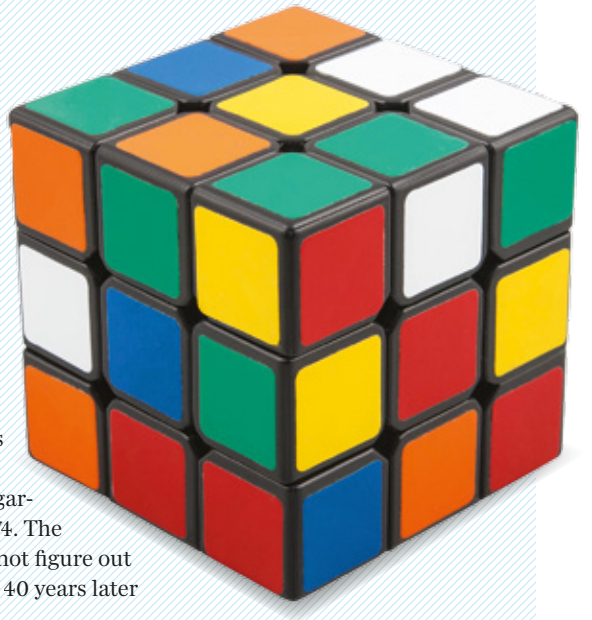
RECOMMENDED

By Clara Moskowitz

MORE TO EXPLORE
WATCH A VIDEO ABOUT RUBIK'S CUBE STRATEGIES AT
SCIENTIFICAMERICAN.COM/NOV2016/RECOMMENDED

Cracking the Cube: Going Slow to Go Fast and Other Unexpected Turns in the World of Competitive Rubik's Cube Solving

by Ian Scheffler. Touchstone, 2016 ($26)



To those who know how, the Rubik's cube can be solved easily in less than 20 seconds. For the rest of us, unscrambling the puzzle at all is next to impossible. Writer Scheffler, who achieved his first "sub-20" time in 2015, takes us inside the world of competitive cubing. He interviews legends such as Jessica Fridrich, who deduced some of the first algorithms for solving the puzzle speedily based on the mathematics of group theory. Fridrich, who was then a teenager in Czechoslovakia, used her solutions to win the nation's Rubik's cube championship in 1982, and the algorithms still dominate competitions today. Scheffler also travels to Budapest to meet the reclusive Erno Rubik, the Hungarian sculptor and architect who designed the cube in 1974. The inventor, a puzzle fanatic then and now, initially could not figure out how to solve his own creation, and he marvels with the author more than 40 years later about the life that the Rubik's cube has taken on in modern years.

Voracious Science and Vulnerable Animals: A Primate Scientist's Ethical Journey

by John P. Gluck. University of Chicago Press, 2016 ($27.50)

In 2015, after a lengthy debate on the ethics of animal research, the U.S. National Institutes of Health announced it would stop using chimpanzees for medical studies and retire its remaining 50 chimps. Gluck, who formerly led his own primate research laboratory, tells the heart-rending personal story of how he became an activist for animal rights. He explains what he calls the "emotional and ethical retraining" that he and other researchers typically undergo as they come up in the field, learning to put aside sympathy for animals in pain. But Gluck soon began to question whether the benefits of animal research truly justify the traumatic cost to its subjects, especially because such studies often fail to translate to human biomedical benefits. He argues that science and ethics cannot be separated and makes the case that a study that would be unethical to conduct on humans is probably unethical to conduct on animals as well. *—Knvul Sheikh*

The Spy Who Couldn't Spell: A Dyslexic Traitor, an Unbreakable Code, and the FBI's Hunt for America's Stolen Secrets

by Yudhijit Bhattacharjee. New American Library, 2016 ($27)

One day in 1999, sitting behind his desk at the National Reconnaissance Office, intelligence agent Brian Regan decided to betray his country. In this true-to-life thriller, writer Bhattacharjee recounts the scheme that Regan concocted to sell thousands of classified U.S. documents about Libyan missile sites, Iraqi air defenses, U.S. spying operations and other secrets. He reached out to potential buyers in coded letters that seemingly contained gibberish. Bhattacharjee examines how FBI agents deciphered these letters and followed clues to Regan's secret identity, such as his military background, which gave him easy access to sensitive reports, his dire need for money and, most important, his poor spelling ability, which finally gave his ciphers away. Bhattacharjee lucidly explains the encryption techniques Regan used to hide information and the mathematics and cryptanalysis that eventually helped FBI agents break the codes. *—K.S.*

The Unnatural World: The Race to Remake Civilization in Earth's Newest Age

by David Biello. Scribner, 2016 ($26)

Planet Earth's 4.5-billion-year history is divided into many geologic epochs, but the latest is unique. The "Anthropocene"—not an official epoch yet but one that many scientists are lobbying for—is named after us (*anthropos* being Greek for "human") because in recent times, we have been the dominant force on the planet. Our cities, farms and factories have redrawn the landscape and crowded out other species, and the carbon dioxide we spew into the atmosphere has changed the global climate, modified the ocean chemistry and transformed Earth in innumerable ways. Journalist Biello, a contributing editor for *Scientific American,* makes an impassioned case for the proposed epoch and describes both what we have done to alter our planet and what we should do in the future to ensure its habitability for people as well as for the many other species that call it home. "The choices made this century," Biello writes, "will help set the course of the entire planet for at least tens of thousands of years."

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

Why Gloom Trumps Glad

The psychology of political pessimism

By Michael Shermer

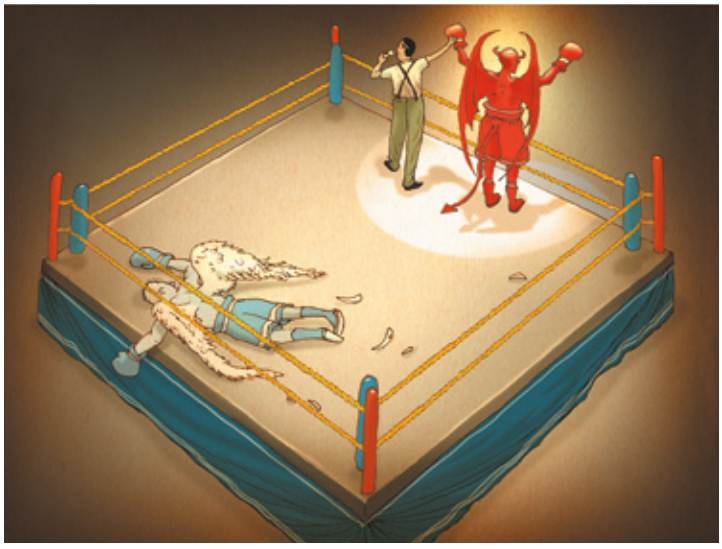
"If you had to choose a moment in time to be born, any time in human history, and you didn't know ahead of time what nationality you were or what gender or what your economic status might be," what time would you choose? Paleolithic? Neolithic? Ancient Greece or Rome? Medieval times? Elizabethan England? Colonial America? The 1950s? "You'd choose today," answered the man who posed this question in an April 2016 speech, President Barack Obama. "We are fortunate to be living in the most peaceful, most prosperous, most progressive era in human history," he opined, adding that "it's been decades since the last war between major powers. More people live in democracies. We're wealthier and healthier and better educated, with a global economy that has lifted up more than a billion people from extreme poverty."

If these facts are true—and they are (see, for example, economist Max Roser's ourworldindata.org and the data at humanprogress.org aggregated from the World Bank, the United Nations, the Organization for Economic Co-operation and Development, and Eurostat)—then why the doom and gloom heaped on us by politicians and pundits on both sides of the political aisle? First, news media outlets are far more likely to report bad news than good, simply because that is what they have been tasked to do. Another day in Turkey without a coup goes unreported, but just try and take over a country without the world's media covering it. Second, as psychologist Roy F. Baumeister explained it in the title of a now classic 2001 paper he co-authored in the journal *Review of General Psychology,* "Bad Is Stronger Than Good." Reviewing a wide range of evidence across many domains of life, the authors found that "bad emotions, bad parents, and bad feedback have more impact than good ones, and bad information is processed more thoroughly than good. Bad impressions and bad stereotypes are quicker to form and more resistant to disconfirmation than good ones." Why?

One answer, I suggest, is in the psychology of loss aversion, in which, on average, losses hurt twice as much as gains feel good. To get someone to take a gamble, the potential payoff must be about twice the potential loss. Why? Because of the endowment effect, which is the tendency to value what we own more than what we do not own. In one experiment, for example, economist Richard Thaler gave subjects a coffee mug valued at $6 and asked them what they would sell it for. The median price was $5.25. Another group of subjects were asked how much they would pay for the same mug. The median price was less than $2.75. Loss aversion and the endowment effect are reinforced by the status quo bias, or the tendency to opt for whatever it is we are accustomed to. For example, we tend to prefer existing personal, social, economic and political arrangements over proposed alternatives.

Why is our psychology wired this way? Evolution. According to Harvard University psychologist Steven Pinker in a 2015 article in *Cato's Letter* on "The Psychology of Pessimism," in our evolutionary past there was an asymmetry of payoffs in which the fitness cost of overreacting to a threat was less than the fitness cost of underreacting. The world was more dangerous in our evolutionary past, so it paid to be risk-averse and highly sensitive to threats, and if things were good, then the status quo was worth maintaining.

All of which helps to explain much political pessimism, such as what we are bombarded with every election. In his book *Moral, Believing Animals* (Oxford University Press, 2003), sociologist Christian Smith reviews the many narratives politicians and pundits construct to reinforce the moral foundations that most concern each side. It boils down to a simple template of "once upon a time things were bad, and now they're good thanks to our party" or "once upon a time things were good, but now they're bad thanks to the other party." Sound familiar? In 2008 Obama campaigned on "change we need" after eight years of a Republican presidency. In 2016 Donald Trump campaigned on making America "great again" after eight years of a Democratic presidency.



As John Stuart Mill observed in 1859: "A party of order or stability, and a party of progress or reform, are both necessary elements of a healthy state of political life." 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.

Muddying the Waters

More of one passenger's science trip down the Colorado River

By Steve Mirsky

The mantra issued by the guides was as clear as the silty Colorado River was opaque: "If you're hot, you're stupid." And so I spent most of my waking hours on and along the river dipping into the 50 degrees Fahrenheit water to counter the 100 degrees F air temperature. I was not hot, but I sure was soaked.

Welcome back for the second part of my tale of the July boat trip through the Grand Canyon with the NCSE, the National Center for Science Education—a trip intelligently designed to include discussions of how scientists see the canyon's formations as billions of years of history written in rock versus how Young Earth creationists see the canyon as evidence for Noah's flood a week ago Thursday. Okay, I'm just kidding. What they believe is that the flood in question happened some 4,400 years ago and produced the geology and fossils of the canyon. Now I'm not kidding. The NCSE works tirelessly to keep that story from being included in public school science classes: Noah … uh, no.

Our group of 25 passengers and crew included the NCSE's Steve Newton, a geologist, and Josh Rosenau, an evolutionary biologist, who discussed the science behind the rock formations, stratigraphy and fossils we saw—and how the aforementioned creationists view the same physical landscape. We got an unexpected taste of that worldview while stopped briefly within the immense Redwall Cavern: two members of the NCSE group overheard a man from a very different tour explaining to his mates that the Almighty cut up big fishes to create little fishes. As Kenneth the page on the NBC sitcom *30 Rock* famously said, "Science was my most favorite subject, especially the Old Testament."

One of the canyon's most obvious points of disagreement between scientists and creationists is what is known as the Great Unconformity—an unconformity is a gap in the geologic record, and this one is pretty great. Under it lies 1.75-billion-year-old rock with the magnificent name of Vishnu Schist. The metamorphic schist is heated and squeezed underneath the earth's surface and gets exposed by uplift and erosion. Directly above the schist is 525-million-year-old Tapeats sandstone. In between is, well, 1.25 billion years conspicuous by its absence.

About halfway through our 226-mile outing, we reached Blacktail Canyon—where visitors can put their hands on that seam in time, only about five feet higher than the ground we walked on. "This is a spot that a lot of creationists come to," Newton said, with the epochal border seam near his elbow. "We've been seeing this Great Unconformity for quite a while—it's been high up in the hills. But this is a spot you can actually come to and touch. From the creationists' interpretation, these are the original rocks of the world—day three, separation of the waters and the land. I can appreciate that it's pretty amazing to touch those rocks. And then the moment of the flood," he said, pointing at the sandstone layer adjoining the schist.

"And that is, you might not be surprised, not what scientists think about all this," Newton continued. "So there's a gap, about 1.2 billion years … you should touch this and realize a quarter of the [history of the 4.5-billion-year-old] world is missing right here … think of all the mountain chains that rose up and then were worn down … and of all the life-forms that lived and died … in that gap."

Try to imagine a billion years passing—our brains may not be up to that task. So I can see how a subset of humanity refuses to buy deep time and believes that everything that ever happened happened to happen in the past six millennia. The First Amendment to the Constitution grants American citizens that right. But as numerous trial verdicts have agreed, that same amendment prohibits the short version of history—and its antievolution corollaries—from being taught in public schools as science. Creationism in biology classes would make our educational system the way I was in the canyon—all wet. SA

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Illustration by Matt Collins

50, 100 & 150 YEARS AGO

INNOVATION AND DISCOVERY AS CHRONICLED IN *SCIENTIFIC AMERICAN*

Compiled by Daniel C. Schlenoff

NOVEMBER

1966 Industrial China

"As a result of the Chinese criticisms of Russian leaders, the U.S.S.R. suddenly withdrew its technical advisers and workers from China in August, 1960. The factories under construction and those already in operation were left without skilled personnel. Faced with the necessity of training her own people to complete the construction projects and run the factories, the Chinese government issued a new slogan: 'Self-development.' From 1960 on China depended largely on her own resources for training engineers, technicians and researchers. She became timid and notably suspicious in her dealings with other countries, Communist or non-Communist, friendly or unfriendly. Her feeling was that those with whom she could trade were out to 'pick her clean.' For this feeling there was some justification, as some of the equipment China had bought from Communist countries turned out to be obsolescent."

1916 Salt Supply

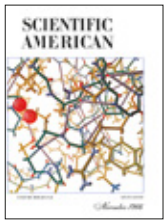
"This city of nearly a million inhabitants is Tzuliutsing in China, the location of the most productive and numerous salt wells of the province of Sichuan and of China. Coming upon this city along the road from the nearest treaty port, Chungking, we at first think that we are approaching an oil well district, for on every side we see tall derricks and hear the squeaking of the pulleys and the driving of the buffalo. The methods in use here are so evidently the prototypes of and in principle the same as those in use in the well drilling and oil fields of America and Europe that one has a great deal of admiration for the ingenuity of the Chinese, who have been using these methods for over a thousand years."

For a slide show of archive images on the history of salt production, see ScientificAmerican.com/nov2016/salt

Steel, Alloys, Research and War

"The business of producing alloy metals, though a virgin field, has sprung into especial prominence because of the necessity of husbanding the supply of iron. The greatest economy in prospect is the use of the rare mineral alloys which produce such a radical increase in strength, coupled with reduction in weight of material consumed. The use of tungsten and vanadium is an old story; the producers of molybdenum now claim for it a future far outreaching that of either of its competitors. It is stated that the great guns with which Germany did such destruction when her artillery preparation took the world by surprise in 1914 were molybdenum guns; that, containing three to four per cent of this substance, their life was twenty times that of the ordinary gun."

1916: Technology of salt extraction in China.



1966

1916

1866

Daylight Saving Experiment

"Although it is too soon to pronounce definite judgment as to the success of the experimental use of 'summer time' in many European countries last summer, the reports thus far at hand are quite uniformly favorable. The United States consul general reports that the Viennese people consumed $142,000 worth less gas under the new time schedule. In England the plan is said to have given general satisfaction, even the farmers, who at first opposed it, having become reconciled."

Electric Cream

"An electrically-operated cream whipper is the latest recruit to the ever-growing army of electrical devices. It consists of a one-gallon hopper, which is equipped with a rotating beater or dasher. The latter member is gear-driven by a one-eighth horse-power motor that may be connected by means of a ten-foot cord to the nearest lamp socket."

1866 Petroleum vs. Sperm Oil

"The *Engineering* says that on the Boston and Worcester, and the Boston and Maine railroads, experiments have been made with petroleum and sperm whale oil to determine which is the best as a lubricator. The results were as follows: They put a railway carriage on each line in perfect order, and used only sperm oil on one truck and only petroleum on the other of each carriage. After running the carriage 19,000 miles, all the axles and brasses were found in good order, with equal wear all round, and 20 per cent less oil had been used from the petroleum cask. They now use petroleum exclusively. This oil, of the best quality, fully equal to pure sperm oil at the least, can now be bought for 50 cents per gallon. Sperm is worth $2.85."

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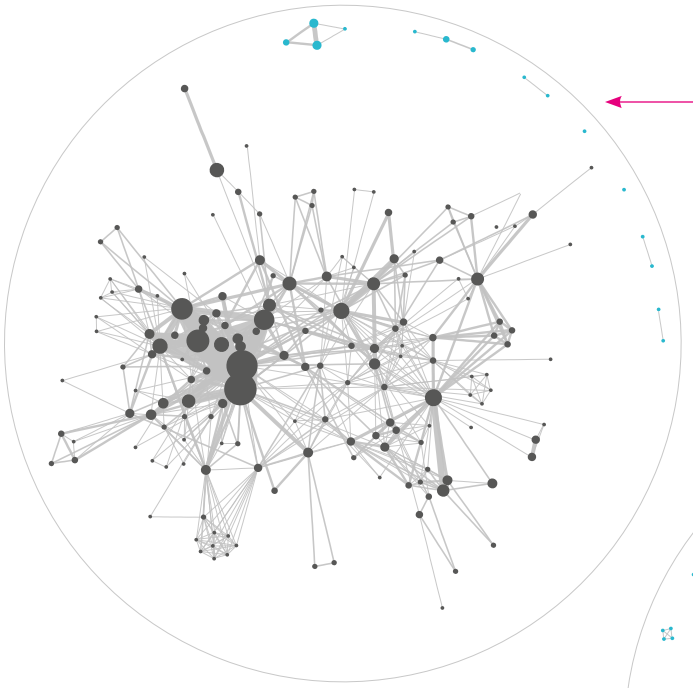
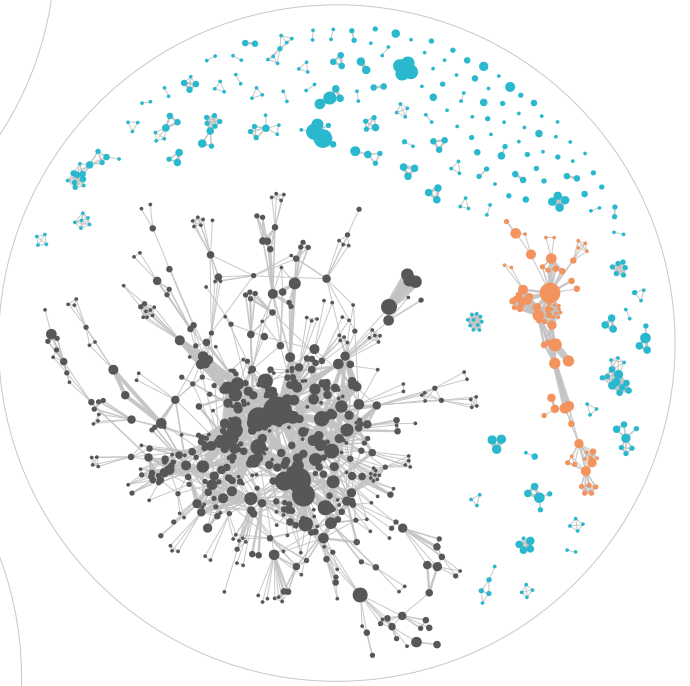
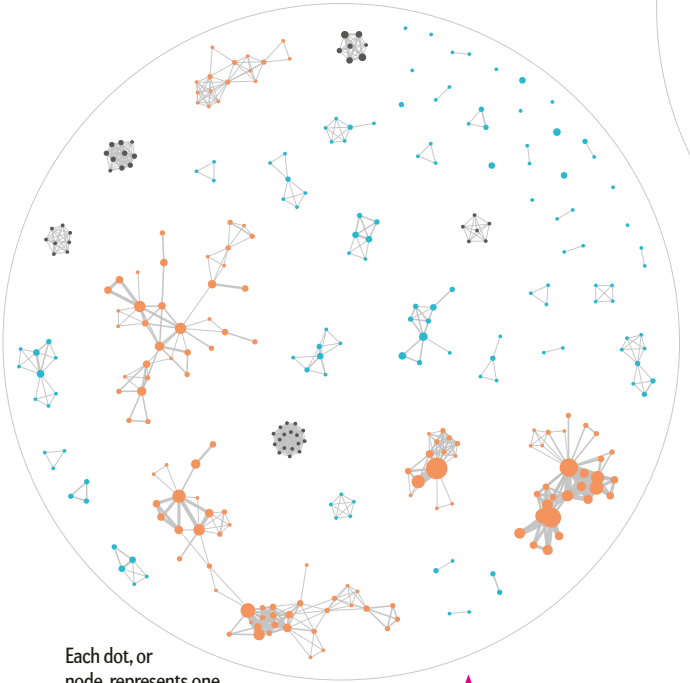


TESLA: The vast majority of inventors form one big collaborative network (*gray*), which includes prolific employees with various patents (*largest nodes*) and individuals who bridge multiple teams (*nodes with many interconnecting lines*). A few employees work mostly alone (*blue*). Tesla appears to rely on a single, complex innovation network in which nearly every inventor is connected to many others, perhaps in part because much of the work is related to battery technology, the heart of the product. Extensive collaboration lets ideas flow rapidly among many innovators.

FACEBOOK: Unlike at Tesla and Intrexon, which are dominated by one pattern, patent holders organize in various ways, perhaps to contribute to different parts of the overall product. One large network has roughly 60 percent of the company's inventors (*gray*), including the most prolific ones (*largest nodes*). Yet a set of employees has formed a relatively large and productive secondary network (*orange*). Others work in smaller, isolated teams.





Each dot, or node, represents one inventor; dot size indicates the number of patents granted to an inventor from 2007 to 2011

· 1 ● 76

Lines connect inventors who share at least one patent; line thickness indicates the number of shared patents (thin = few, thick = many)

Clusters of dots show inventors who work closely together

INTREXON: The inventor network has several sizable teams, which appear to work in seclusion (*clusters of different colors*). Many inventors also work alone or in isolated pairs or triads. Overall, the innovative network is highly fragmented, perhaps because the company develops specialized products that differ from one another.

The Many Ways to Innovate

Patent data show that companies have very different strategies for invention

Numerous books have been written about how businesses innovate, but most rely on case studies. The U.S. Patent and Trademark Office recently took a more data-driven look. It analyzed patents for employees at three large tech companies in varied fields: Tesla (*top*) in electric vehicles, Facebook (*right*) in social networks and Intrexon (*bottom*) in genetic engineering. How employees team up to invent patented technologies reveals different patterns of collaboration, says senior economist Amanda Myers at the patent office. Given how well each of these companies is doing, it seems that there is more than one way to create success. *—Mark Fischetti*

SOURCES: U.S. PATENT AND TRADEMARK OFFICE AND WWW.PATENTSVIEW.ORG

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1884

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