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Afflicting millions of women
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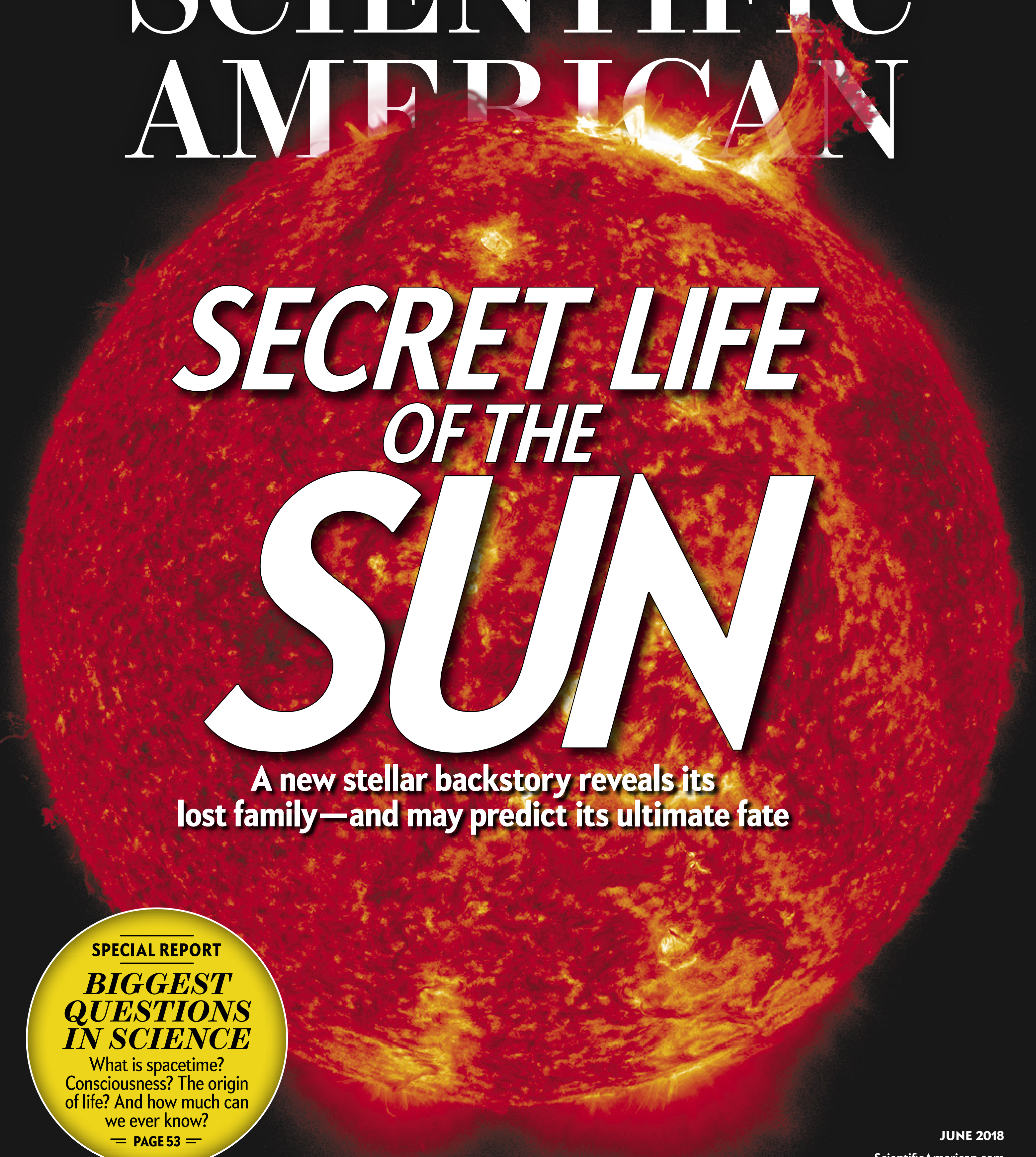
SCIENTIFIC AMERICAN



SECRET LIFE OF THE SUN

A new stellar backstory reveals its lost family—and may predict its ultimate fate

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ScientificAmerican.com

QUALITY CONTROL AT THE CUTTING EDGE OF PHARMACEUTICAL SCIENCE

A conversation with **JAAP VENEMA**, Chief Science Officer for USP

USP has been creating standards for the quality of medicines, published in the *United States Pharmacopeia – National Formulary*, for nearly two centuries. Their task today is more challenging than ever, with new kinds of medicines, cutting-edge technologies and an ever-expanding global pharmaceutical marketplace. Jaap Venema, Ph.D., Chief Science Officer for USP, explains how his organization stays at the forefront in developing quality standards for this rapidly evolving field.

How does USP define quality in the context of medicines?
If you go to the pharmacy and get your prescription, you probably don't give a second thought to what that product is or what the quality is—and that's because organizations like USP exist. Much of what impacts the quality of medicine goes on behind the scenes. Many factors determine the quality of the final product, including all of the materials that go into the process and the conditions during manufacturing. To determine quality, we ask four questions. *Identity*—is the product what it claims to be? *Potency*—is the active ingredient present in the right amount? *Purity*—what impurities are present and in what amounts? And finally, *performance*—will it dissolve in the body and do what it's supposed to do?

How does USP collaborate with the global community to set these standards?
USP is an independent scientific organization, working with a large body of scientific volunteers—currently over 750—from many different places, countries, and areas of expertise and from different types of organizations: academia, industry, practitioners, government, *et cetera*. They develop new standards, and revise and modernize existing standards. In this work, our volunteer experts act as individual scientists and do not represent their employer or any other organization. Another important aspect of our process is that there is always an opportunity for the public to comment on the development of USP standards. So literally anybody on the planet can provide comments on anything we propose. This is a vital part of our process.

With pharmaceutical technology evolving so rapidly, how does your organization keep up?
Innovations in manufacturing technology and testing continually push the science of standards, and that is a never-ending cycle. Our research and innovation team works to identify what quality will look like in the future and to identify ways we will continue to safeguard it. Today we are focusing on innovations such as 3D printing and continuous manufacturing.

How will continuous manufacturing be important in the pharmaceutical industry?
It has already been employed in various industries, such as the chemical, food, and auto industries, but not to a great extent in pharmaceuticals. Continuous manufacturing is attractive because it provides a closed system that can offer both flexibility and consistency in product manufacturing. Visualize a juice machine, where as long as you're feeding oranges into the top, juice will come out the bottom. It never stops, but you are able to adapt the process to changing conditions. Let's say the oranges you put in at the beginning contain less sugar than usual, you can adapt the process in the machine to adjust the water vs. sugar content so that you still have the same product rolling out at the end. Right now, pharmaceutical manufacturing uses a technique called 'batch processing.' Manufacturers create each 'batch' of a product by doing one step, and then the next step, going to the next machine, and so on, with all of the holding times in between and even sometimes changing facilities. In batch processing there are many opportunities for quality to be compromised. Continuous manufacturing can help improve quality, and it is something being actively promoted by the FDA. We have formed an expert panel that is exploring how quality standards can be applied to the closed system of continuous manufacturing, which comes with a new set of challenges regarding analytical technologies.

USP standards are recognized in the US, but how is your organization working to ensure standards are applicable and relevant in a globalized drug supply chain?
Our standards are used in approximately 140 countries, and that is helpful. We also work across borders with a number of regional or global organizations, as well as directly with other pharmacopeias around the world to try to harmonize standards wherever possible. The other piece that is very much related to standard-setting is strengthening of quality systems worldwide. This is a complex endeavor that involves convening and collaborating with stakeholders around the globe; working on the ground in individual countries to expand the skilled workforce, working with local manufacturers to help them produce products to international standards, and working with health ministries and regulators to monitor and test products. Combined, these efforts help ensure the quality of medicines in their local market and ultimately in the interconnected global market.

Hundreds of volunteer scientists work together to help USP establish quality standards that build a foundation for a healthier world. Learn more at usp.org/together.

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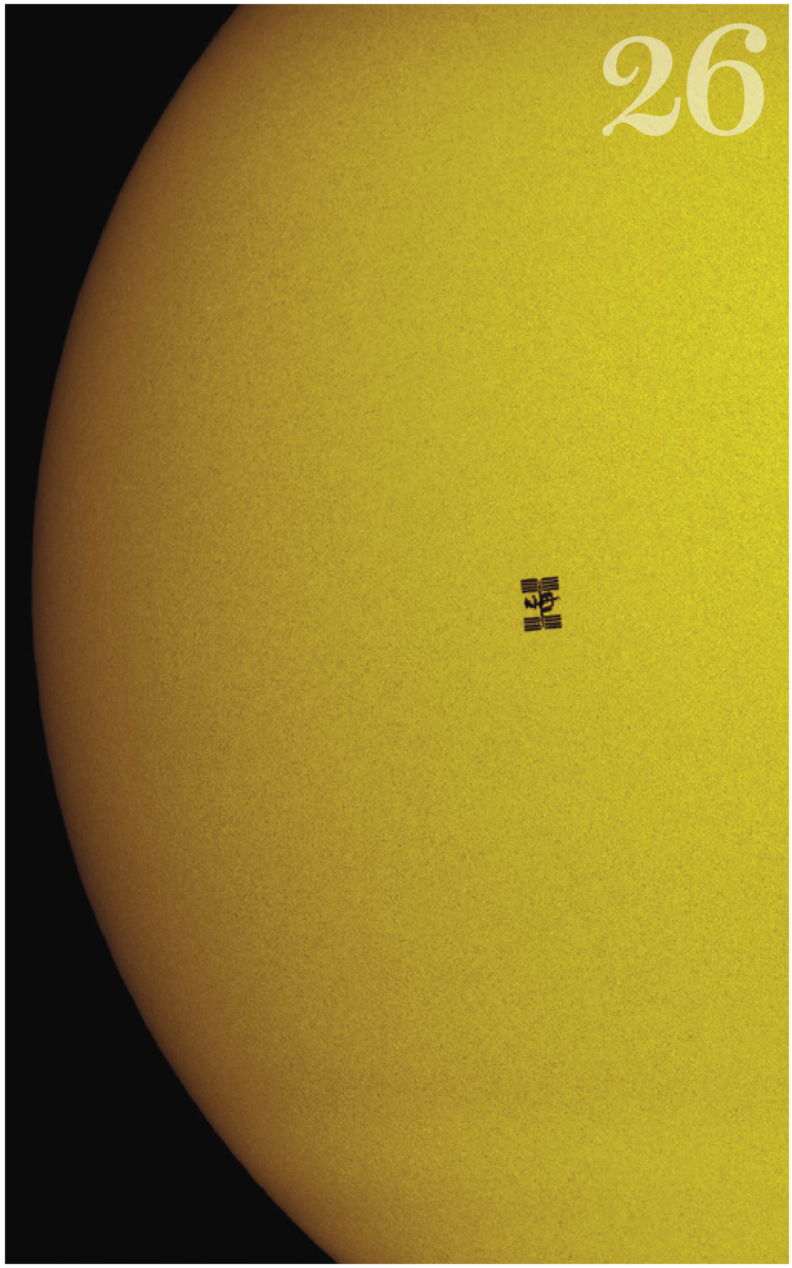
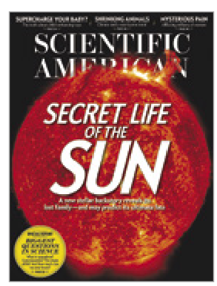


THIERRY LEGAULT (*solar transit of International Space Station*)

ON THE COVER
The sun, shown in this 2014 image from NASA's orbiting Solar Dynamics Observatory, has had a tumultuous life. Recent research has revealed details about its stellar ancestors and siblings, its natal environment and evolution, and its eventual demise. **Photograph by NASA's Solar Dynamics Observatory and AIA, EVE and HMI science teams.**



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ON THE WEB

New Audio Stories

Scientific American now offers audio versions of some Advances articles on the 60-Second Science podcast. The first one describes surprising geologic activity in New England.

Go to www.ScientificAmerican.com/jun2018/advances_podcasts

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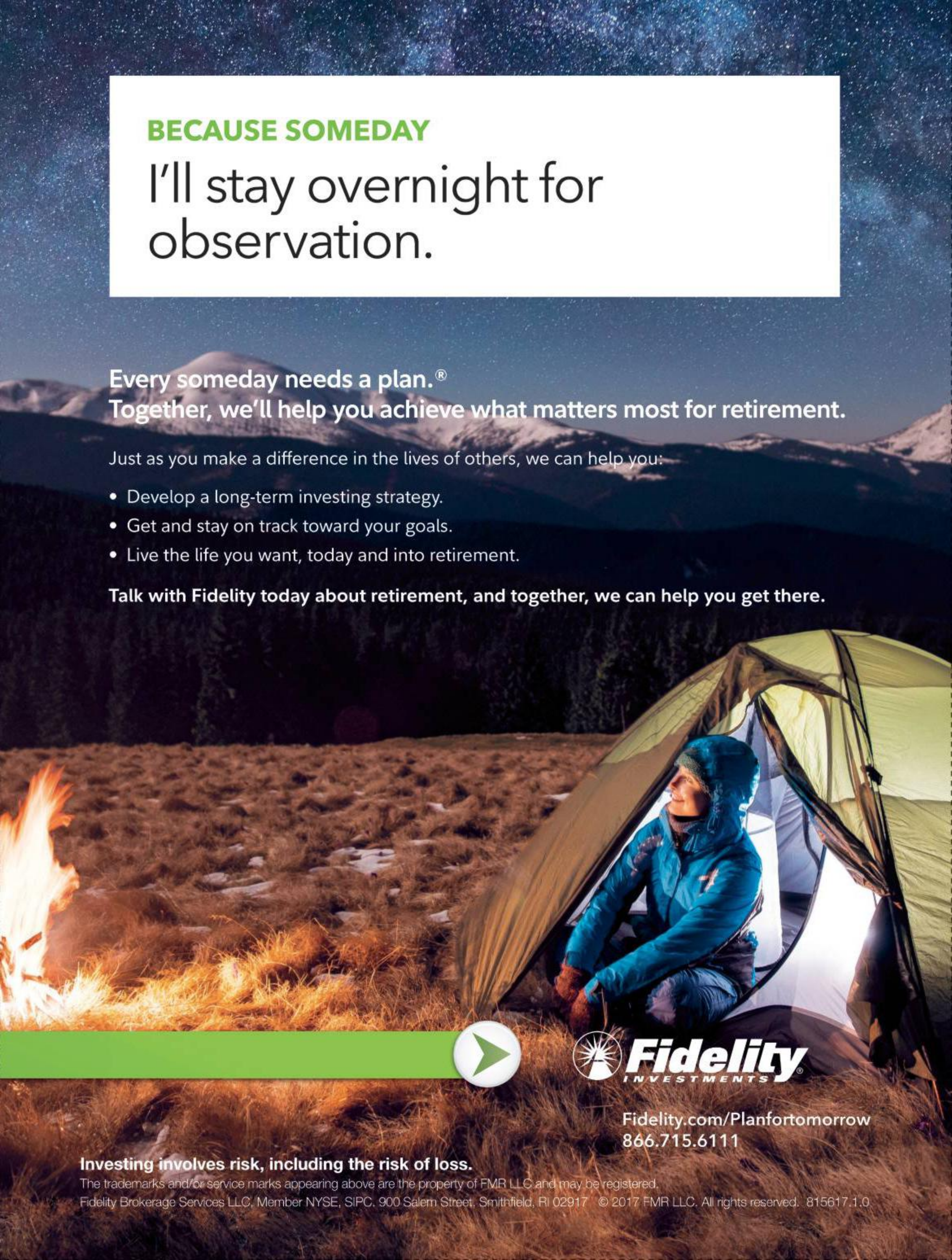

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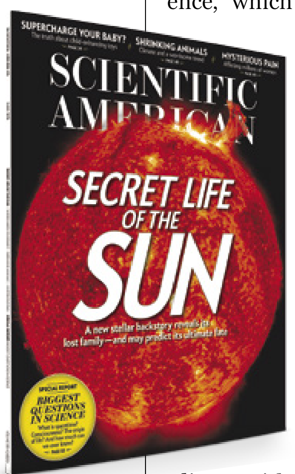
FROM THE EDITOR

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

The Sun, Supercharging and the Search

I have always been captivated by science's seemingly inexhaustible ability to produce new findings. And my favorite insights often require some mental time travel and also involve mysteries surrounding objects we think we know well. This month's cover story offers a bit of intellectual candy in providing both. In "The Secret Life of the Sun," journalist Rebecca Boyle winds back the cosmic clock to our friendly neighborhood star's younger years. In that earlier era, we learn, our sun had a "mother," "aunts" and "uncles"—even "siblings"—now residing elsewhere in the Milky Way. Our sun may have stolen a planet from a relative. And when it dies, perhaps it will help "birth" a future star. Begin your celestial journey on page 26.



In the realm of human births, what are parents to make of the numerous marketing messages on playthings and games offering to help their babies to learn and even to walk sooner? On page 34, journalist Erik Vance asks, "Can You Supercharge Your Baby?" Vance writes that although play is important for development, unfortunately little science backs up claims of supercharging tots with toys. We parents and caregivers remain the best educators for helping little ones learn how to navigate the world.

Whether it is the start of life for our sun or for our sons and daughters, science's ability to ask how things work drives how we are advancing discovery. Along these lines, I would like to point you to a special section on "The Biggest Questions in Science," which begins on page 53. This report, part of an occasional series called Innovations In, which is being published by both *Scientific American* and our sister title, the journal *Nature,* examines some of the most fundamental puzzles of our existence.

Contributing editor George Musser kicks off the section with his feature on "What Is Spacetime?" Other articles explore consciousness (by neuroscientist Christof Koch), nanoscience (journalist Neil Savage), dark matter (theoretical physicist Lisa Randall) and life's origins (biologist and Nobel laureate Jack Szostak). Rounding out the package, theoretical physicist Marcelo Gleiser asks the existential question, "How Much Can We Know?" This collaboration was developed independently by *Scientific American* and *Nature* editors, with the support of the Kavli Prize, which is celebrating the 10th year since the first Kavli Prizes honoring great minds who have looked at the world around them and wondered: Why? We may never know all the answers to our questions, but we are happy to join in cultivating humanity's eternal pursuit of knowledge. ■

Illustration by Nick Higgins

February 2018

HEAVY HOLES

I was puzzled by one aspect of "The First Monster Black Holes," Priyamvada Natarajan's article on the oldest supermassive black holes: If there were a substantial number of such black holes in the early universe, observable today at great distances, what happened to them? Would we not see them, and the quasars they produce, nearby in the modern universe?

Jean Renard Ward *via e-mail*

Supermassive black holes have been found at the centers of spiral galaxies. Given that they are many times larger than previously thought, is "dark matter" still needed to hold those galaxies together?

Bruce Emerick *Carriere, Miss.*

NATARAJAN REPLIES: In response to Ward: We do see monster black holes around us in the nearby universe. Almost every galaxy near us harbors a central black hole, and the brightest ones host the most massive black holes. But these local monsters are no longer feeding on gas, so they do not glow as quasars. Instead they are detected by their impact on the motions of stars in their vicinity, which are sped up. By measuring the speeds, we can infer the presence of the dormant but strong gravitational grip of the black hole and can actually estimate its mass.

To answer Emerick: Indeed, supermassive black holes are found ubiquitously, including at the centers of spiral galaxies. Despite the fact that these central black holes are supermassive, their region of influence is limited: stars eventually overtake them in mass in the inner regions of galaxies and start to dominate gravitationally. Alas, these behemoths are insufficient to hold the rest of the galaxy together—their gravity dominates only a small region. And to explain the rotational speeds of stars in the outer regions of galaxies, we require vast amounts of dark matter.

"One of the most significant drivers for physicians to carry out procedures such as surgeries is economics."

THOMAS W. ADAMS *FORT WORTH, TEX.*

SURGICAL DECISION

"Why Fake Operations Are a Good Thing" [The Science of Health], Claudia Wallis's article on sham surgeries used to evaluate operations, omits one of the most significant drivers for physicians to carry out procedures, whether they be surgery or something less invasive, and that is economics. It is not possible for physicians to make nearly as much per hour seeing, counseling or prescribing drugs for patients.

Thomas W. Adams *Fort Worth, Tex.*

CONFLICT ANALYSIS

In "The Tribalism of Truth," Matthew Fisher, Joshua Knobe, Brent Strickland and Frank C. Keil claim that "contemporary political discourse is becoming more combative and focused on winning." Are we to believe that politics is more combative now than it was during the days of the Whiskey Rebellion, the American Civil War, William Jennings Bryan's "Cross of Gold," McCarthyism, desegregation, busing, *Roe v Wade* and the Vietnam War?

Politics have always been combative, and whether it is decided by votes or arrows, the first-place finisher gets the power—with no silver medal for coming in a strong second.

Lou Eisenberg *via e-mail*

The authors argue that the world is divided into objectivist and relativist views on answers to moral or political questions and that an objectivist outlook is linked to arguing to win, whereas a relativist one is linked to arguing to learn. It seems to me that a third outlook is possible: that of the objectivist learner. Indeed, the basis of the scientific method is to assume that there is an objective truth or reason behind observable phenomena, which a series of well-designed experiments can elucidate.

An open and frank dialogue about things for which there is no objective truth, such as whether veggie cream cheese is tasty, is another way of learning: opinion learning. The difficulty comes when an objective truth is treated as an opinion, or vice versa. Doing so hampers learning.

Paul M. Kioko *via e-mail*

PHARMA CHUMS?

In "[Redacted]," his article on the Food and Drug Administration possibly withholding certain drug trial data, Charles Seife suggests that the FDA may "block evidence of outcome switching and even hide references to a medication's side effects" to protect a pharmaceutical company's competitiveness. But that's not the whole story. For an upper-level director in a government agency, there is also the prospect of a high-paid position, on or before retirement, with the very companies that the agency is mandated to supervise.

David Werdegar *Naperville, Ill.*

LIGHT FEAR

"Are Smartphones Really Destroying the Adolescent Brain?" by Carlin Flora, is a timely and balanced look at research on smartphone usage in adolescents. As the article notes, studies have associated overuse with a number of negative effects in teenagers, but association is not causation.

In addition to the concerns Flora reports, I might note that before the 20th century, the human retina was not exposed to flashes of light as fast as those on any computer screen. It is conceivable that this massive daily exposure to quick flashes could cause interruption of pathways in the growing brain. Studies using advanced brain imaging might provide a convincing mechanism if and how this damage might occur. Further, several years ago Dimitri Christakis of the University of Washington compared groups of newborn mice exposed to simulated TV lights and sound with a control group and found that prolonged exposure diminished the quality of essential survival functions in the exposed group.

Karl Berger *Johnstown, Pa.*

UNIVERSAL VACCINE

In "A Universal Flu Vaccine Is Vital" [Forum], Catharine I. Paules and Anthony S. Fauci warn that seasonal vaccines are inadequate protection against a future pandemic flu. But developing a vaccine against all strains is not only vital to reduce the suffering from a pandemic per se. In the U.K., during the winter of 2017–2018, tens of thousands of scheduled operations were postponed because hospitals were being overwhelmed by infections with the current influenza strain (a relatively small number compared with what might be expected from a pandemic). Demography suggests that such problems can only be predicted to increase.

Peter B. Baker *Prestwood, England*

VAN GOBOT

David Pogue's article on AI-created art, "The Robotic Artist Problem" [TechnoFiles], seems to miss the value of art altogether. We are interested in the *Mona Lisa* because of what it tells us about Leonardo da Vinci, about his subject and, more important, about their relationship. A creation by a robot would only be of interest with respect to what we learn about the human engineer who created it because we are social creatures drawn to relationships and the characters in them.

Christa Helms *via e-mail*

PUBLIC OUTREACH

In "Go Public or Perish" [Science Agenda], the editors decry universities discouraging scientists from speaking to the public. We live in a society that is based on science but is made up of politicians and voters who are largely scientifically illiterate. It is the duty of scientists to help them understand what we know or are learning. We don't need to be salespeople, but we should explain the difference between scientific evidence and sensationalism or denial.

Randy Oliver *Grass Valley, Calif.*

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Who Owns the Dead?

The law that allows Native Americans to claim ancient remains must be stronger

By the Editors

On February 18, 2017, more than 200 members of five Native American tribes gathered at a secret location on the Columbia Plateau in Washington State to return the remains of the Ancient One to the earth. The homecoming was two decades in the making for the roughly 9,000-year-old skeleton, also known as Kennewick Man, which was discovered in 1996. It had been delayed by a bitter dispute between scientists who wanted to study him and tribes who claimed he was their ancestor and wanted to rebury him, in keeping with their religious customs.

The battle raged for as long as it did in part because it was not clear whether the federal law governing the return of Native American remains to tribes that can demonstrate a cultural connection to them applied to remains as old as the Ancient One. The law defines Native American as "of, or relating to, a tribe, people, or culture that is indigenous to the United States." In 2004 scientists who had sued to prevent repatriation of Kennewick Man won their case because a judge deemed the skeleton too old to be considered Native American. Ever since then, tribes and anthropologists have called for the law's definition of Native American to be amended to include previously existing indigenous groups, along with current ones. Ongoing discoveries of bones, artifacts and DNA from deep time add new urgency to this imperative.

For centuries white explorers and settlers in the Americas dug up the graves of indigenous people, looting sacred artifacts and using the remains for studies that promoted white superiority. The Native American Graves Protection and Repatriation Act (NAGPRA) was passed in 1990 to enable tribes to protect and recover their heritage, and it has succeeded in reuniting many items from federally funded institutions with their rightful custodians. But when remains cannot be culturally linked to a modern tribe—or no tribe claims them—scientists may conduct research without getting approval from tribes to do so.

Yet advances in DNA technology mean that remains once thought to be "culturally unidentifiable" will increasingly be linked to modern groups through genetics, as ultimately happened in the case of the Ancient One, whose DNA revealed a close genetic affiliation to one of the five claimant tribes. And although genetic ties alone do not determine affiliation, they are a strong line of evidence. NAGPRA must be updated to reflect this technological reality by clarifying that it applies to ancient remains.

Simply following the letter of the law is not good enough, however. Just a few days after the reburial of the Ancient One, researchers announced results of genetic analysis of bones from New Mexico's Chaco Canyon. The bones are housed at the American Museum of Natural History in New York City. The DNA results suggested that a maternal "dynasty" ruled at Chaco for hundreds of years and gave rise to the matrilineal organization of modern Pueblo groups. But as *Scientific American* reported at the time, the museum's scientists did not consult modern tribes before extracting DNA from the remains because the museum deemed the bones impossible to link to any specific group. They should have invited input from tribes, both out of respect for their overarching concerns about ancestors and because collaboration might have enriched the study—through the addition of tribal knowledge about kinship systems, for example, or through comparative DNA samples from any modern tribes interested in providing them.

Scientists have a moral obligation to seek out those who might have a connection to the remains of the dead and let them decide their fate. They might not always like the decision—tribes may decide to prevent or restrict study of the remains—but they have more to gain than to lose from such cooperation. In January researchers reported the recovery of DNA from bones of an infant girl who had been buried in Upward Sun River, Alaska, some 11,500 years ago. Before studying her remains, the team obtained approval for DNA sequencing from the Athabascans who live at Upward Sun River today and asked them what questions they had about the find. That partnership led to the revelation that the skeleton represented a previously unknown branch of Native Americans and that the site contains the oldest evidence of salmon fishing in the Americas—an important tradition to Athabascans.

Giving Native peoples a voice in the study of their heritage is the only way to heal the wounds of the past—and build the trust needed to move forward together with scientists toward a fuller understanding of the human story.

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Illustration by Cornelia Li

Peter Salovey is president and Chris Argyris Professor of Psychology at Yale University.

Knowledge Can Be Power

Only if colleges and universities teach *all* students to think like scientists

By Peter Salovey

If knowledge is power, scientists should easily be able to influence the behavior of others and world events. Researchers spend their entire careers discovering new knowledge—from a single cell to the whole human, from an atom to the universe.

Issues such as climate change illustrate that scientists, even if armed with overwhelming evidence, are at times powerless to change minds or motivate action. According to a 2015 Pew Research Center survey, people in the U.S., one of the countries that emits the most carbon, were among the least concerned about the potential impact of climate change. Why are so many Americans indifferent to this global threat? Yale University professor Dan M. Kahan and his colleagues reported in *Nature Climate Change* that people with the "highest degrees of science literacy and technical reasoning capacity were not the most concerned about climate change."

For many, knowledge about the natural world is superseded by personal beliefs. Wisdom across disciplinary and political divides is needed to help bridge this gap. This is where institutions of higher education can provide vital support. Educating global citizens is one of the most important charges to universities, and the best way we can transcend ideology is to teach our students, regardless of their majors, to think like scientists. From American history to urban studies, we have an obligation to challenge them to be inquisitive about the world, to weigh the quality and objectivity of data presented to them, and to change their minds when confronted with contrary evidence.

Likewise, STEM majors' college experience must be integrated into a broader model of liberal education to prepare them to think critically and imaginatively about the world and to understand different viewpoints. It is imperative for the next generation of leaders in science to be aware of the psychological, social and cultural factors that affect how people understand and use information.

Through higher education, students can gain the ability to recognize and remove themselves from echo chambers of ideologically-driven narratives and help others do the same. Students at Yale, the California Institute of Technology and the University of Waterloo, for instance, developed an Internet browser plug-in that helps users distinguish bias in their news feeds. Such innovative projects exemplify the power of universities in teaching students to use knowledge to fight disinformation.

For a scientific finding to find traction in society, multiple factors must be considered. Psychologists, for example, have found that people are sensitive to how information is framed. My research group discovered that messages focused on positive outcomes have more success in encouraging people to adopt illness-prevention measures, such as applying sunscreen to lower their risk for skin cancer, than loss-framed messages, which emphasize the downside of not engaging in such behaviors. Loss-framed messages are better at motivating early-detection behaviors such as mammography screening.

Scientists cannot work in silos and expect to improve the world, particularly when false narratives have become entrenched in communities. This is especially true in tackling issues such as public trust in vaccines, a topic that is flooded with misleading information, despite a lack of legitimate scientific evidence supporting the view that they are unsafe. Interdisciplinary research groups worldwide are investigating this global challenge. For example, computer scientists worked with a psychologist to understand people's attitudes in social media toward vaccination, and an international team tracked worldwide sentiments toward immunizations using data-driven methods. These findings inform community and policy discussions that are based on facts and understanding of one another's concerns, not on assumptions.

Universities are conveners of experts and leaders across disciplinary and political boundaries. Knowledge is power but only if individuals are able to analyze and compare information against their personal beliefs, are willing to champion data-driven decision making over ideology, and have access to a wealth of research findings to inform policy discussions and decisions. SA

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Illustration by Matt Harrison Clough

ADVANCES

A fire in Ventura County, California, in 2017. A growing number of homes are at risk from such conflagrations.

INSIDE

MARCUS YAM *Getty Images*

ENVIRONMENT

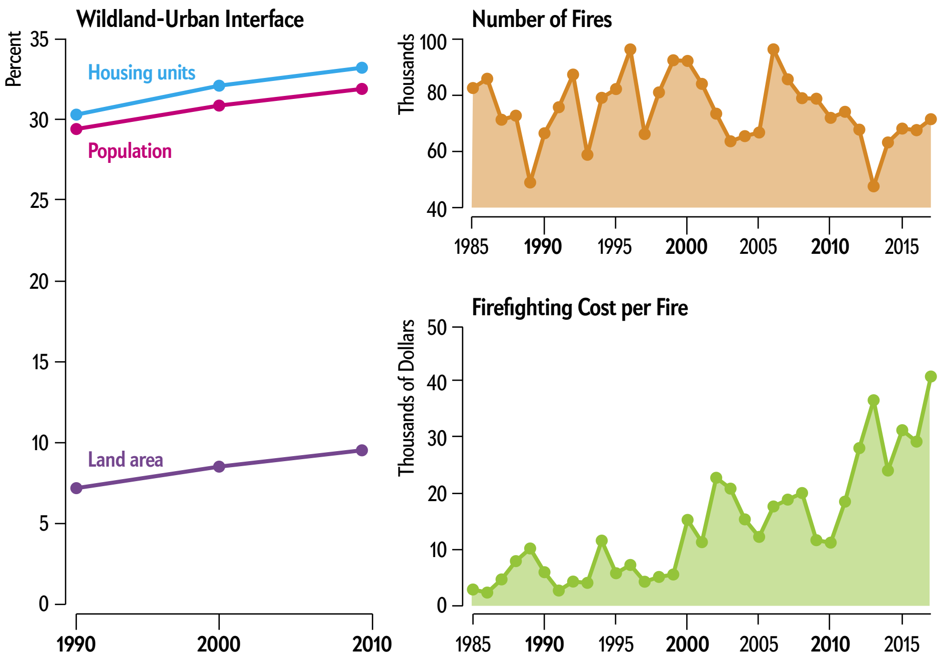
Into the Wildfire

Building houses at the edge of the wilderness increases the danger of catastrophic blazes

The horrific Tubbs Fire in California's Sonoma and Napa counties last October tore through more than 36,000 acres, killing 22 people and destroying nearly 6,000 buildings. It was the most destructive wildfire in the state's history in terms of structures lost, according to the California Department of Forestry and Fire Protection.

Half a century earlier the Hanley Fire burned some 53,000 acres along a nearly identical path. Although that blaze remains Sonoma County's largest on record, it destroyed only a few dozen structures, most of which were homes. The main difference between then and now is the expansion of what researchers call the wildland-urban interface, or WUI: the area where houses sit within or directly adjacent to natural vegetation.

The WUI in the U.S. increased by 33 percent between 1990 and 2010, to about 190 million acres, according to a study published in March in the *Proceedings of the National Academy of Sciences USA*. The number of houses within the WUI grew by 41 percent in the same period, an addition



The wildland-urban interface (WUI) refers to the zone in which houses are built in or near wilderness areas. It can be measured in terms of its land area, the number of housing units it contains or the number of people living in it. By all three metrics, the WUI in the U.S. has increased steadily in recent years. The annual wildfire count in the WUI has not changed significantly during this time, but the price of suppressing each fire has skyrocketed. This is largely the result of WUI growth: more buildings in the paths of fires can make managing outbreaks harder. Warming temperatures and other climate change–related factors have also contributed to rising costs.

of nearly 13 million new homes. Having more structures in the WUI increases not only the damage wildfires inflict (because they are harder to fight) but also the risk that they will break out in the first place. "The Forest Service is concerned about more and more houses built in and near wildland vegetation because of this double whammy," says the study's lead author Volker Radeloff, a forest ecologist at the University of Wisconsin–Madison.

Sonoma County was sparsely populated when the Hanley Fire struck in 1964. But thousands of people settled there in the following decades, eager to live out their vision of the American dream, complete with a backyard and white picket fence. Nationwide, the total WUI now comprises an area larger than Washington State and includes approximately one in every three houses. This trend may reflect homeowners' desire to be close to nature, but wildfires in this kind of landscape pose a greater threat to people and to the economy than they do elsewhere.

Between 1990 and 2010 the U.S. population grew by 60 million, and the nation added nearly 30 million homes, but it was previously unclear how much of that increase occurred within the WUI. Nor was it clear whether WUI growth was the result of the construction of new homes or of the recovery of natural ecosystems alongside areas that had already been developed. In the new study, Radeloff and his team combined census data with satellite imaging to quantify WUI growth since 1990. Understanding why and how the WUI expands is critical for evaluating wildfire-management policies, especially given the tremendous economic burden such fires impose.

The number of acres burned by wildfires each year has increased slightly over the past few decades, but the amount of taxpayer dollars that federal agencies spend on fighting them has grown sharply. In 2017 that bill ran to $2.9 billion—$2.4 billion of it footed by the U.S. Forest Service alone. Although the agency's fire-suppression costs have more than tripled since the early 1990s, its budget has not kept pace.

"If they're spending a significant chunk of their [total] budget on fire management, they're not spending it on other things," says fire ecologist Jennifer K. Balch of the University of Colorado Boulder, who was not involved in the study. For example, lands managed by the Forest Service contribute around a fifth of the nation's water supply; for California, they contribute almost half. Focusing its resources on firefighting leaves the agency with less money to maintain and restore watersheds.

"We now have lots more people literally living in the line of fire," Balch adds. "Are people expecting federal agencies like the [Forest Service] to protect all these homes? If that's the case, then we really have to think about our dedicated budgets for fire-suppression costs." Balch notes that the WUI's growth is accelerating, with no sign of slowing down. "In a lot of places in the U.S., it's not a question of *if;* it's a question of *when* will that home be exposed to wildfire," she says.

Although there are steps that homeowners and developers can take to mitigate that danger (such as using more flame-resistant construction materials and making more appropriate landscaping choices), Radeloff says municipal leaders need to begin incorporating fire risks into their plans. Rather than attempting to prevent fires from occurring, perhaps it is wiser to anticipate those that are inevitable. Communities can be more fire-adapted by resisting the temptation to allow building on high-risk plots, he argues—"and that hasn't happened yet, at least not at broad scales." This is unfortunate, Radeloff says, "because we know that fires will continue, and climate change will bring weather conditions conducive to large fires more frequently in the future." Various solutions to the problem of building in the WUI have been proposed, but to date none have stopped people from tempting nature's fiery whims. *—Jason G. Goldman*

SOURCES: "RAPID GROWTH OF THE US WILDLAND-URBAN INTERFACE RAISES WILDFIRE RISK," BY VOLKER C. RADELOFF ET AL., IN *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES USA*, VOL. 115, NO. 13; MARCH 27, 2018 (*WUI data*); NATIONAL INTERAGENCY FIRE CENTER (*fire and cost data*)

Graphic by Amanda Montañez

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1

2

Worker bee brood (*1*) and a honeybee hatching (*2*).

ANIMAL PHYSIOLOGY

Deathly Scent

Chemical odors trigger honeybees to remove their dead

A dozen years ago beekeepers started reporting that frightening numbers of their honeybees (*Apis mellifera*) were mysteriously dying. Scientists have since discovered multiple reasons, but "diseases are by far the main cause of problems with honeybee health right now," says Leonard Foster, professor of biochemistry and molecular biology at the University of British Columbia. The insects are afflicted by scourges ranging from varroosis (caused by mites) to the bacterial disease American foulbrood. Now a new study reveals how the smell of dead honeybees could be used to help identify and breed healthier colonies.

Scientists have long known honeybees remove dead or diseased individuals from among their young, or "brood," to restrict the spread of pathogens through a colony. British Columbia researcher and study lead author Alison McAfee, along with Foster and other colleagues, wanted to better understand why some colonies are more fastidious about this cleanup than others are. They selected two chemicals naturally produced by honeybees, oleic acid and beta-ocimene, whose odors they thought might act as cleanup signals. Many insects release oleic acid at death, and honeybee larvae release beta-ocimene to signal their need for food. Young honeybees emit both compounds when they die.

The researchers performed a series of tests to determine if these odors were connected to hygienic behavior. In one experiment, they added oleic acid and beta-ocimene to a live brood developing in comb cells, in an attempt to trick worker bees into thinking the brood was dead. The workers removed more brood members from cells doused with a blend of both chemicals, compared with insects exposed to only one of the odors or to a control chemical, the team reported in April in *Scientific Reports.* The researchers think that beta-ocimene alerted workers to attend to the brood and that oleic acid triggered them to remove the "dead."

The team also found a link between the odors and the genetics that drive honeybees' hygienic behavior. Because some bees appear to respond more strongly to "death" smells by cleaning, these findings may help scientists develop a better way to breed more hygienic bees. "The fact that they have a mechanism by which the bees can identify these smells—and they actually get a plausible mechanism with their genetics—is really exciting," says Jay Evans, a research scientist at the U.S. Department of Agriculture, who was not involved in the study. "If validated, there could be a way to measure that trait, so that beekeepers could select a bee breed that's hygienic based on genetics." —*Annie Sneed*

GETTY IMAGES (*1*); INGO ARNDT *Getty Images* (*2*)

PALEONTOLOGY

Suffocated Seas

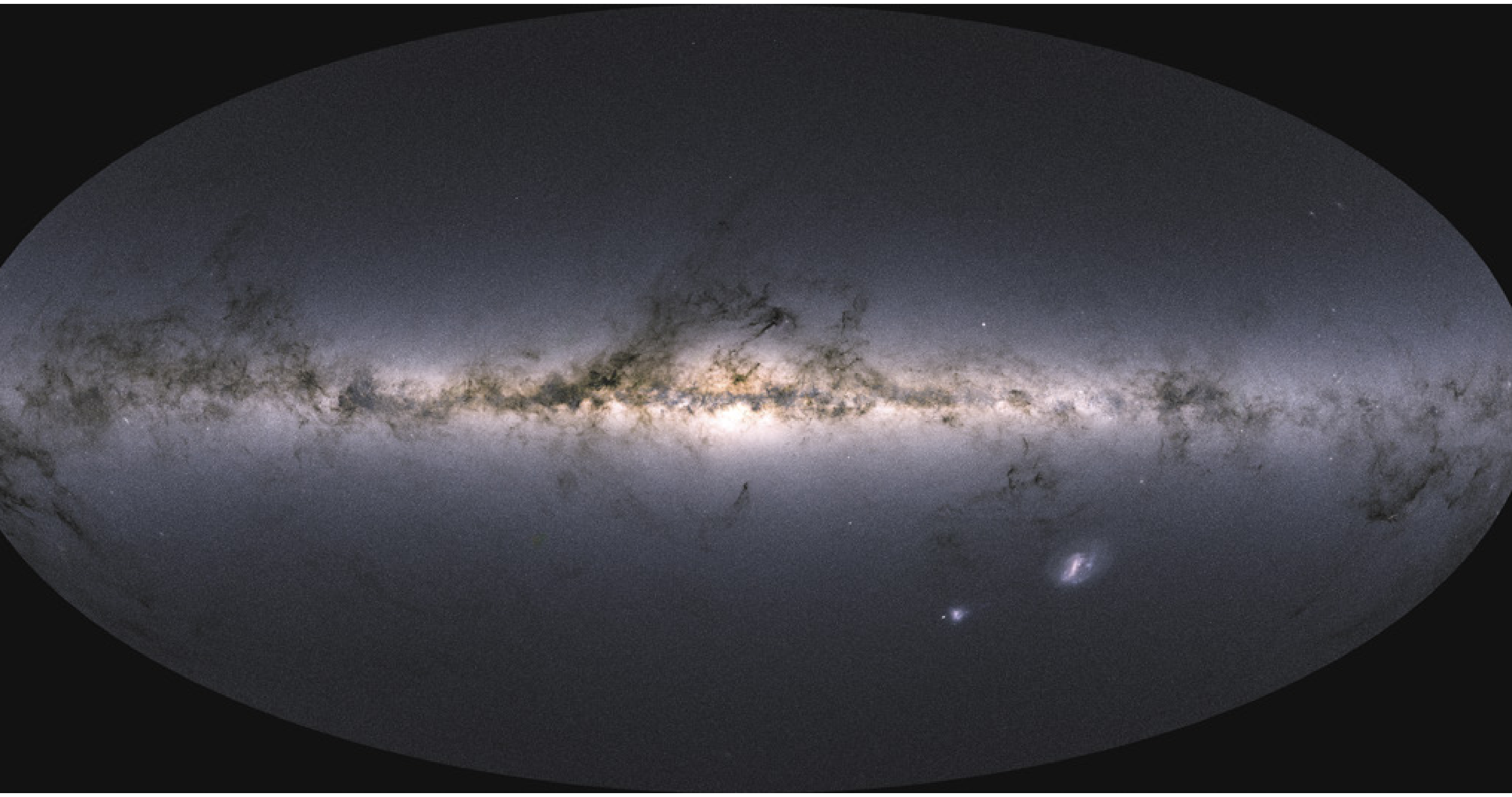
Researchers pinpoint driver of massive marine life die-off

Earth's largest mass extinction to date is sometimes called the Great Dying—and for good reason: it wiped out about 70 percent of life on land and 95 percent in the oceans. Researchers have long cited intense volcanism in modern-day Siberia as the main culprit behind the cataclysm, also known as the Permian-Triassic mass extinction, 252 million years ago. A recent study pins down crucial details of the killing mechanism, at least for marine life: oceans worldwide became oxygen-starved, suffocating entire ecosystems.

Scientists had previously suspected that anoxia, or a lack of oxygen, was responsible for destroying aquatic life. Supporting data came from marine rocks that formed in the ancient Tethys Ocean—but that body of water comprised only about 15 percent of Earth's seas. That is hardly enough to say anything definitive about the entire marine realm, says Feifei Zhang, a geochemist at Arizona State University, who led the new research.

In contrast, Zhang says, "our data point to a rapid, global intensification of marine anoxia during the Permian-Triassic mass extinction." The key to the team's finding, which was published in April in *Geology,* is a novel method that uses uranium measurements in rocks to infer ancient oceanic oxygen levels. This approach enabled the researchers to spot clues in rocks from Japan that formed around the time of the extinction in the middle of the Panthalassic Ocean, which then spanned most of the planet and held the majority of its seawater. "The most exciting thing is the ... global signature they're seeing," says Gregory Brennecka, a geochemist at the University of Münster in Germany, who was not involved in the study.

The findings may have special relevance in modern times because the trigger for this ancient anoxia was most likely climate change caused by Siberian volcanoes pumping carbon dioxide into the atmosphere. And today, as human activity warms the planet, the oceans hold less oxygen than they did many decades ago. Brennecka cautions against speculating about the future but adds: "I think it's pretty clear that when large-scale changes happen in the oceans, things die." —*Lucas Joel*



An all-sky map of the Milky Way galaxy, based on observations from the ESA's Gaia mission.

SPACE

Milky Way Remapped

New data offer an unprecedented look at the galaxy's stars

In an eagerly anticipated development, astronomers have created the largest and most precise 3-D map of the Milky Way galaxy. The European Space Agency's $1-billion Gaia mission released its newest data set in April, detailing the positions and motions of more than a billion stars.

The Gaia spacecraft, launched in 2013, scans the entire sky from its orbital parking spot above the side of Earth opposite the sun. Its unprecedented map is based on 25 separate observations of individual stars and their movements over about two years and contains a representative sample of 1 percent of the Milky Way's orbs. The data, described in a series of papers published online starting in April in *Astronomy & Astrophysics,* can be extrapolated to simulate the galaxy's past and future.

"We are measuring a map in a moment in time, but we can also go backward and forward," says Jos de Bruijne, Gaia's deputy project scientist.

Gaia released its first data set in September 2016. But because of limited observation time and reliance on prior knowledge of celestial positions, it tracked the distances and motions of only two million stars. The second data set contains similar details on 1.3 billion of them—650 times as many as the initial trove.

The telescope can accurately observe stars in the galactic center, up to 30,000 light-years away—equivalent to a person on Earth spotting a penny on the moon. "The precision of the proper motions measured by Gaia is what really makes it so revolutionary," says Allyson Sheffield, an astrophysicist at LaGuardia Community College, who was not involved in the project.

Gaia's two optical telescopes and three scientific instruments can also measure stellar brightness, temperature and composition. The new data set includes stars' colors, which can reveal crucial details about their surface temperature and age. Such diverse observations make the spacecraft a "one-stop galactic-structure shop" for astrophysicists, Sheffield says.

The data also include the radial velocities—the motions toward or away from Earth—of seven million stars. Such measurements allow scientists to calculate the speed of these orbs with respect to our sun, which in turn reveals more about how the galaxy may have evolved. As a bonus, the data set contains observations of 14,099 asteroids orbiting within the solar system.

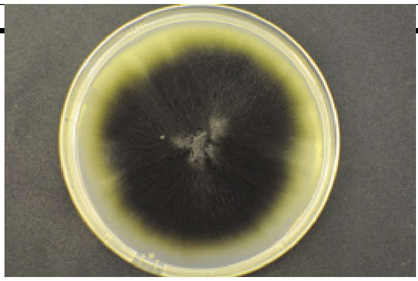
Precise knowledge of stellar motions will not only improve scientists' understanding of galactic history and evolution, it could also offer clues to the nature and distribution of mysterious "dark matter" and could test alternative theories of gravity, says Amina Helmi, an astrophysicist at the Kapteyn Astronomical Institute in the Netherlands and a member of the ESA's Gaia mission. *—Jeremy Hsu*

EUROPEAN SPACE AGENCY, GAIA, AND DATA PROCESSING AND ANALYSIS CONSORTIUM

MICROBIOLOGY

Frozen Fungi

Antarctic microorganisms produce intriguing new chemical compounds



BENJAMIN HELD *University of Minnesota*

Antarctica might seem an unlikely place to find microbes that degrade wood. The icy continent has no trees, and it lacks the warm, damp conditions typically associated with decomposition. But in recent years several species of fungi have been found on wood structures built there by Ernest Shackleton and other early 20th-century explorers. Scientists grew some of these unusual organisms in the laboratory and found they produced never before seen chemicals—which researchers are now investigating for potential applications in medicine.

Robert A. Blanchette, a forest pathologist at the University of Minnesota, and his colleagues traveled to Antarctica eight times to sample these fungal specimens. Fungi are the basis for many drugs, including the antibiotic penicillin, the immunosuppressant cyclosporine and the cholesterol buster lovastatin, so Blanchette wondered if these Antarctic species might produce any useful molecules. He teamed up with Christine Salomon, a chemist at the university's Center for Drug Design, to analyze them. Salomon was working off the hypothesis that microorganisms living in harsh, nutrient-starved environments need to "protect their turf" and often maintain a competitive edge over other fungi or bacteria by making antimicrobial compounds. These chemicals could potentially be transformed into much needed pharmaceutical therapies.

In a study published in April in *Phytochemistry,* Salomon grew several species of the Antarctic fungi *Cadophora* and found they produced nine compounds new to science. None of the compounds proved effective at killing human pathogens in lab tests, nor were they toxic to two types of mammalian cancer cells, however. Although Salomon admits this result was "really surprising and kind of disappointing," she says it does not necessarily rule out some medical potential.

One species her team tested made exceptional quantities of a compound called colomitide C—about 1,000 times the concentration of similar compounds she is accustomed to finding in fungi and bacteria. In subsequent, unpublished work, the compound stopped the growth of rapidly regenerating tissue in zebra fish, suggesting an indirect role in inhibiting some fast-growing tumors. Salomon's group also found preliminary evidence showing that colomitide C reversed the growth of breast cancer cells in mice, and her colleagues are now attempting to replicate the findings.

—*Peter Andrey Smith*

CHEMISTRY

Quirky Graphene

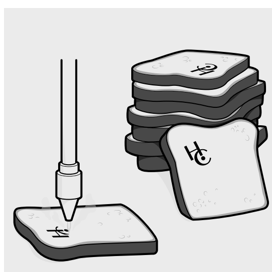
The versatile carbon material has some new tricks up its sleeve

Graphene seems to be a gift that keeps on giving. This much hyped material, which consists of a one-atom-thick layer of carbon and is the basic unit of graphite, is known for its strength, conductivity and other useful properties. It holds promise for a slew of futuristic uses, from high-capacity batteries to lighter and stronger aircraft wings. It is slowly finding its way to market in conductive inks and specialty sports gear. But other proposed applications are closer to home: some researchers think graphene could revamp everything from personal care to footwear.

NANO HAIR DYE

Graphene sheets can cling to one another and appear black, as graphite does. So could they be used to color hair? To find out, materials scientist Jiaxing Huang and his colleagues at Northwestern University mixed graphene flakes in water with chitosan, an edible sugar made from crustacean shells. When they brushed the resulting ink on blond hair samples, the pliable flakes wrapped tightly around the hairs' curved surfaces; the chitosan glued the carbon in place by binding with the hair protein keratin. The dye lasted for 30 washes, the researchers reported in April in *Chem.*

Store-bought permanent dyes work via a string of chemical reactions "using your head as a flask," Huang says. The harsh chemicals can damage hair and irritate skin. Graphene's possible health and environmental risks are still being studied, but the dye is nonabrasive, and the flakes are too large to enter human pores, Huang notes. And the material's resistance to electrostatic charge bestows a nice side effect: it fights frizz.



ELECTRONIC ID TAGS

Zap fabric or food with a laser, and it chars. By doing so in a carefully controlled way, researchers rearranged carbon atoms in natural materials into graphene. As described in a study published online in February in *ACS Nano,* scientists seared graphene patterns into cloth, paper and even bread. This technique could potentially etch electronic circuits that would act as biodegradable radio-frequency identification (RFID) tags for tracking apparel or banknotes. It could also create edible sensors that would indicate if fruit was ripe or contaminated.

Rice University chemist James Tour, the study's senior author, says the laser's intense light and heat rearrange carbon atoms and form bonds among them. Multiple passes are key. An initial blast singes the material to create amorphous carbon, or soot. Subsequent passes organize the atoms into graphene's signature honeycomb pattern.

FANCY FOOTWEAR

Extra-gripping graphene shoes may be sprinting into stores this year. British sportswear company Inov-8 plans to sell running shoes that have rubber soles spiked with the wonder material, which should make them stronger and more flexible.

Italian shoemaker Fadel has gone a step further. Teaming up with researchers at the Italian Institute of Technology in Genoa, the company added graphene to its Freshoes sandal outsoles and insoles. The material purportedly imparts antimicrobial properties and wicks away heat, keeping feet fresh and cool. —*Prachi Patel*

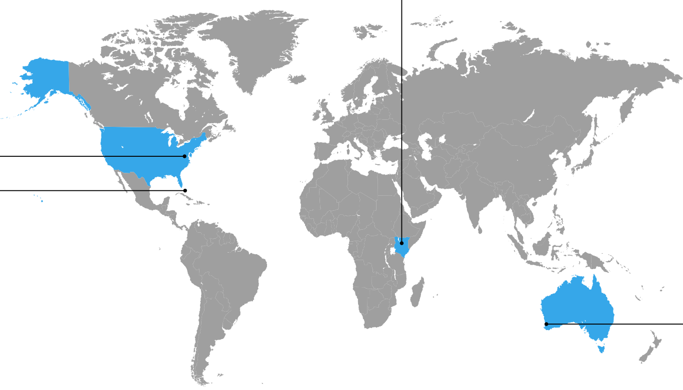
Illustrations by Brown Bird Design

IN THE NEWS
Quick Hits

U.S.
A viral Twitter post led to the identification of an African-American woman among a large group of men in an archival photograph from a 1971 whale biology conference in Virginia. The only person unidentified, she turned out to be Sheila Minor—a biological research technician with a 35-year scientific career.

KENYA
The world's last male northern white rhino, called "Sudan," died in March at age 45 (the equivalent of about 90 for humans). Only two females of the subspecies, Sudan's daughter and granddaughter, remain.

BAHAMAS
DNA from the 1,000-year-old tooth of an indigenous Taino woman, excavated on the island of Eleuthera, suggests at least one modern Caribbean population is related to her. The finding contradicts a theory that the Taino went extinct after contact with Europeans.

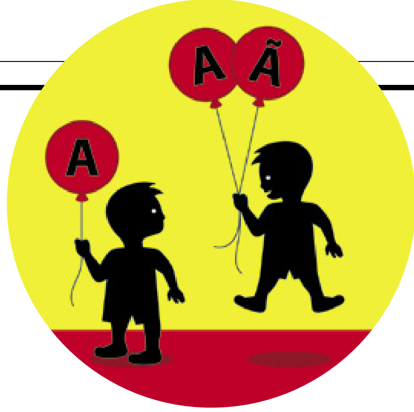


AUSTRALIA
A fisher discovered around 150 stranded whales on a Hamelin Bay beach, prompting a major rescue effort that saved only five. Biologists do not know what causes stranding behavior but think it may happen when the animals are sick, injured or lost.

ANTARCTICA
Using satellites, drones and ground surveys, scientists spotted a previously unknown population of 1.5 million Adélie penguins thriving on the Danger Islands near the Antarctic Peninsula. This species has been declining in many other parts of the continent.

—Yasemin Saplakoglu

For more details, visit www.ScientificAmerican.com/jun2018/advances



COGNITIVE SCIENCE

Bilingual Boost

Speaking a second language may give low-income kids a leg up

Children growing up in low-income homes score lower than their wealthier peers on cognitive tests and other measures of scholastic success, study after study has found. Now mounting evidence suggests a way to mitigate this disadvantage: learning another language.

In an analysis published online in January in *Child Development,* Singapore Management University researchers probed demographic data and intellectual assessments from a subset of more than 18,000 kindergartners and first graders in the U.S. As expected, they found children from families with low socioeconomic status (based on factors such as household income and parents' occupation and education level) scored lower on cognitive tests. But within this group, kids whose families spoke a second language at home scored better than monolinguals.

Evidence for a "bilingual advantage"—the idea that speaking more than one language improves mental skills such as attention control or ability to switch between tasks—has been mixed. Most studies have had only a few dozen participants from mid- to high-socioeconomic-status backgrounds perform laboratory-based tasks.

Andree Hartanto, a doctoral candidate at Singapore Management University and the study's lead author, says he sought out a data set of thousands of children who were demographically representative of the U.S. population. It is the largest study to date on the bilingual advantage and captures more socioeconomic diversity than most others, Hartanto says. The analysis also includes a real-world measure of children's cognitive skills: teacher evaluations.

The use of such a sizable data set "constitutes a landmark approach" for language studies, says Jon Andoni Duñabeitia, a professor at Nebrija University in Madrid, who was not involved in the work. But Duñabeitia notes the data did not contain details such as when bilingual subjects learned each language or how often they spoke it. Without this information, Hartanto concedes, it is difficult to draw conclusions about how being bilingual could confer cognitive advantages.

Kenneth Paap, a psychologist at San Francisco State University, thinks other factors may explain higher performance in bilingual children. For example, they are more likely to be immigrants. Previous epidemiological studies have revealed a "healthy immigrant effect," Paap says, referring to findings that immigrants on average have better physical health and lower mortality rates than native-born citizens. This benefit could extend to cognitive ability.

Hartanto agrees that it will take more work to untangle the complex relations among bilingualism, socioeconomic status and cognitive development. The new findings, he says, "show us that the answer to bilingual cognitive advantages should not be a simple yes or no." —*Jane C. Hu*

HEALTH

Couch Potato Persona

Prolonged physical inactivity may make people less agreeable

A sedentary lifestyle has long been linked to poor health, and a growing body of evidence suggests it may also affect personality. Previous research found associations between a lack of exercise and declines in character traits such as conscientiousness, measured four to 10 years after initial surveys. Now the largest analysis of its kind to date has used longer follow-up periods to confirm these links and show they persist up to nearly two decades.

A team led by psychologist Yannick Stephan of the University of Montpellier in France reached this conclusion after combining data from two large, survey-based studies. The Wisconsin Longitudinal Study (WLS) followed people who had graduated from that state's high schools in 1957, as well as some of their siblings. The Midlife in the United States (MIDUS) study recruited people from across the country. Participants in both had completed personality questionnaires when first recruited in the 1990s and answered questions about their exercise habits and health.

Nearly 20 years later a total of about 9,000 people took the same surveys again. Stephan and his team found that subjects who reported being less active had greater reductions on average in conscientiousness, openness, agreeableness and extroversion—four of the so-called Big Five personality traits—even after accounting for differences in baseline personality and health. No link was found with the fifth trait, neuroticism. The changes in traits were small, but the link with exercise was relatively strong. Physical activity predicted personality change better than disease burden did, for example. The findings were published in April in the *Journal of Research in Personality.*

Numerous mechanisms may be involved—from physiological factors such as stress response to changes in physical ability that can affect how much people socialize. "Personality is, in part, what [behaviors] we repeatedly do, and changes in habits can consolidate into changes in personality," says epidemiologist Markus Jokela of the University of Helsinki, who was not involved in the new study.

Correlations do not prove causation, however. Additional factors, such as genetics or earlier life events, might be affecting both exercise levels and personality. The findings also need to be replicated in samples from different cultures and in studies using objective measures of an active lifestyle.

Nevertheless, the new analysis underscores the idea that personality is malleable throughout life. It also tallies with studies suggesting personality is linked to health. "These findings further emphasize the need for physical activity promotion in midlife and older age," Stephan says. —*Simon Makin*

Illustration by Thomas Fuchs

Claudia Wallis is an award-winning science journalist whose work has appeared in the *New York Times, Time, Fortune* and the *New Republic.* She was science editor at *Time* and managing editor of *Scientific American Mind.*

Why We Won't Miss Opioids

They are not the great all-purpose painkillers they've been cracked up to be

By Claudia Wallis

Erin Krebs started medical school in 1996, just months after OxyContin was approved for sale in the U.S. Over the next seven years, as she earned her M.D. and trained in internal medicine, she watched in astonishment as "oxy" and other potent opioids became the reflexive prescription for all manner of pain while worries about addiction and prolonged use were brushed aside. "As a natural skeptic, I went looking for a good reason why we changed our practice," she recalls, "and it wasn't there."

It was then that Krebs conceived of a "dream study" that, amazingly, had never been done: a long-term randomized controlled trial comparing opioids with nonopioids for treating serious chronic pain. It took a while, but with funding from the U.S. Department of Veterans Affairs, Krebs, now at the Minneapolis VA Health Care System, began such a study in 2012, after enrolling 240 veterans who suffered from persistent moderate-to-severe back pain or a similar level of arthritic pain in their hips or knees.

Patients were randomly assigned to either an opioid group or a nonopioid group, both starting with low-intensity drugs but able to move to stronger stuff as needed. The results, published in March, were eye-opening. Patients given alternative drugs did just as well as those taking opioids in terms of how much pain interfered with their everyday life. In fact, they reported slightly less pain and had fewer side effects.

Why hadn't such a study been done before? "At some level, physicians, as well as the general public, were willing to believe we don't need studies to show us that these drugs work," Krebs suggests. Powerful drug-marketing efforts had somehow swamped science. Dentists were also caught up in the rush to opioids. Apart from Tylenol with codeine, they had been reluctant to offer such drugs before the 1990s, says Harold Tu, director of oral and maxillofacial surgery at the University of Minnesota School of Dentistry. Now about 95 percent of dentists and oral surgeons prescribe hydrocodone or oxycodone for patients undergoing painful procedures, such as wisdom tooth extraction.

Like Krebs, Tu was not convinced that opioids were a superior choice. Dental research said otherwise. He was also horrified by the possibility that his profession had helped open the gateway to today's opioid addiction crisis, which caused more than 42,000 overdose deaths in the U.S. in 2016. "The evidence shows that dentists—and in particular, oral surgeons—are one of the largest prescribers to people between ages 10 and 19," he notes. Research also shows that high school students who are prescribed opioids have a 33 percent increased risk of later misusing the drugs.

In early 2016, under Tu's leadership, the Minnesota dental school introduced a mandatory protocol stipulating that the first-line treatment for pain would be nonsteroidal anti-inflammatory drugs such as high-dose ibuprofen. Opioids were permissible after a difficult surgery, but providers had to use the lowest adequate dose and register the prescription in a digital tracking system.

The result: in 15 months the school's 30 practitioners cut opioid prescriptions nearly in half, according to a report to be published later this year. Nevertheless, they saw no increase in after-hours calls or return visits related to pain. Since the study was completed, opioid use has further plummeted, Tu says: in 2015 95 percent of painkillers prescribed after a procedure were opioids; in 2017 it was just 21 percent. The average number of opioid pills per patient also dropped—an important change because unused pills often go astray. Surveys show that dentists typically prescribe 16 to 24 opioid pills, and yet patients use about eight.

Changing practice isn't easy, even in the face of a crisis. The amount of opioids prescribed in the U.S. fell by 18 percent between 2010 and 2015—not nearly enough—and the number of pills per script actually rose! Krebs is a firm supporter of using opioids for acute surgical pain or for easing the agony of dying, but there has never been good evidence for deploying them against chronic pain. And yet colleagues told her it would be "unethical" to withhold the drugs from patients in her study. Patients may also balk. Some told Tu, "The only thing that works is Vicodin."

I know how that is. Last year I was stunned when my periodontist presented me with a script for 800-milligram tablets of ibuprofen following surgery in which she sliced tissue from my palate and stitched it to my gums. "Is this all I need?" I mumbled incredulously through the novocaine. "You'll be fine," she told me. And indeed, I was. SA

Illustration by Celia Krampien

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

Apps We Really Need

The Waze model of crowdsourced info is only the beginning

By David Pogue

Ordinarily, I love transatlantic flights. Sure, there's something magical about being transported to another land. But there's also something deliciously self-indulgent about watching all the movies you want, without paying for them or feeling guilty about the time you're spending on them.

That's why, on a recent flight to London, I was irked to discover that my seat-back screen was busted.

Yeah, I know: #firstworldproblem. Still, in this world of instant information about anything, it's too bad there's no app that would let me warn whoever sat in 22F on this plane's *next* flight about the broken screen. (Or, conversely, where the *previous* occupant of my seat could have warned *me*.)

The concept of real-time, crowdsourced reporting isn't so far-fetched. Consider Waze, the GPS navigation app (now owned by Google). Its killer feature: drivers can report what they encounter on the road to other Waze-equipped drivers. Traffic jams, police cars, accidents, stopped cars, speed traps, road closures, and so on.

When Waze debuted, nobody had the app, so nobody reported anything, so nobody needed it. I actually doubted it would ever catch on, and without the so-called network effect, the app would be worthless. But somehow it flew, and now millions of people have made Waze an incredible info source for anyone who drives.

Once when I took my kids to Disney World, I was delighted to discover an app that employs exactly the same trick to tell you how long the lines are at each ride. (It's called—surprise—Wait Times for Disney World.) Where does this information come from? Fellow park visitors, doing their part to help one another by tapping in the wait times they're experiencing.

This idea—real-time communication of temporary conditions to fellow citizens—is so powerful, simple, useful and obvious, I'm amazed that it is not more common. So here, for the benefit of all humankind, especially app developers looking for ideas, I'm pleased to offer seven great new Waze-like app ideas.

City Sleep Saver. How many times has your hotel room sleep been ruined because of construction noise from a building nearby (or even within the hotel)? For me, it's *very* often. The hotel sure isn't going to warn you—but this app will.

Garage Guru. By the time you've snaked your way through the parking lot or garage trying to find a spot only to discover that there isn't one, you've missed the beginning of your dinner or meeting. Never again! Now the last driver to pull in can alert the world that the lot is full.

Movie Movers. Why should *anyone* ever suffer the disappointment of turning up at a sold-out movie? With one tap in this app, people already at the theater can indicate that certain times are full. If they're especially kind, they'll even tell you when they see that *other* movies are sold out besides the one they were going to. The same app should have an option to report projection problems, sticky floors or overzealous air-conditioning.

TSA Tsk-Tsk. Sometimes you breeze through airport security and wind up cooling your heels at the gate; other times the line is bafflingly long, and you risk missing your flight. But with this app, you'll know ahead of time how bad the lines are.

Black Friday Bulletin. Every Black Friday, stores advertise a few incredible deals—loss leaders, like a particular TV model at 60 percent off, for example. Only after you've fought the crowds and made it into the store do you discover that they had only 10, and they're gone. If only you'd known!

Tinder Loving Care. It's so handy that Tinder can help you find a date. Now we need an app that, after you've just finished with a date that was vile or abusive, lets you warn the next person who's tempted to swipe right.

Restroom-Ready. What's more irritating than a public bathroom stall that's out of toilet paper or a sink without soap? With this app, you'll know before you go.

Having the right data at the right time and place could make all our lives more efficient, less expensive and better-lived. Waze had the right idea. Now let's spread it. SA

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Illustration by Jay Bendt


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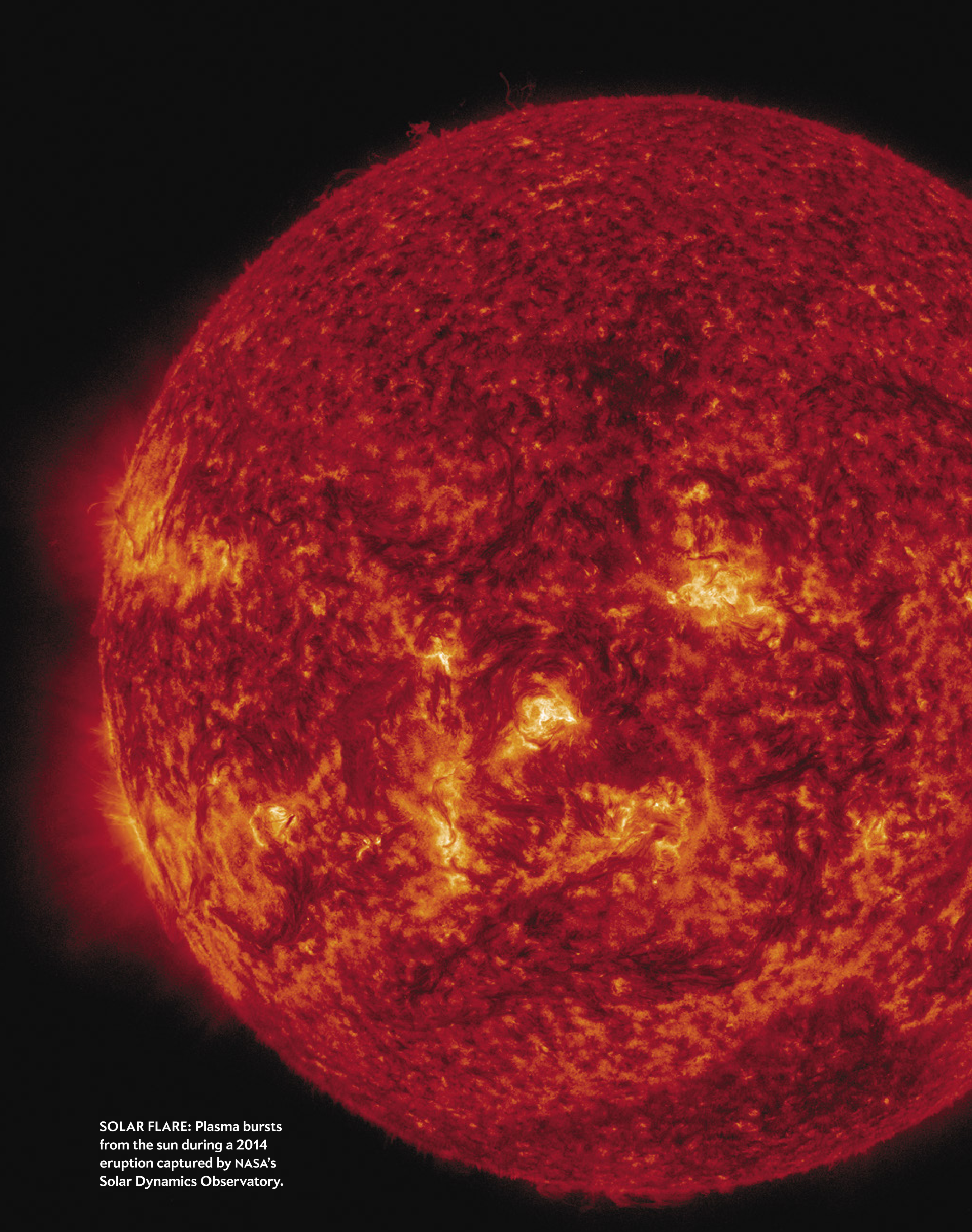
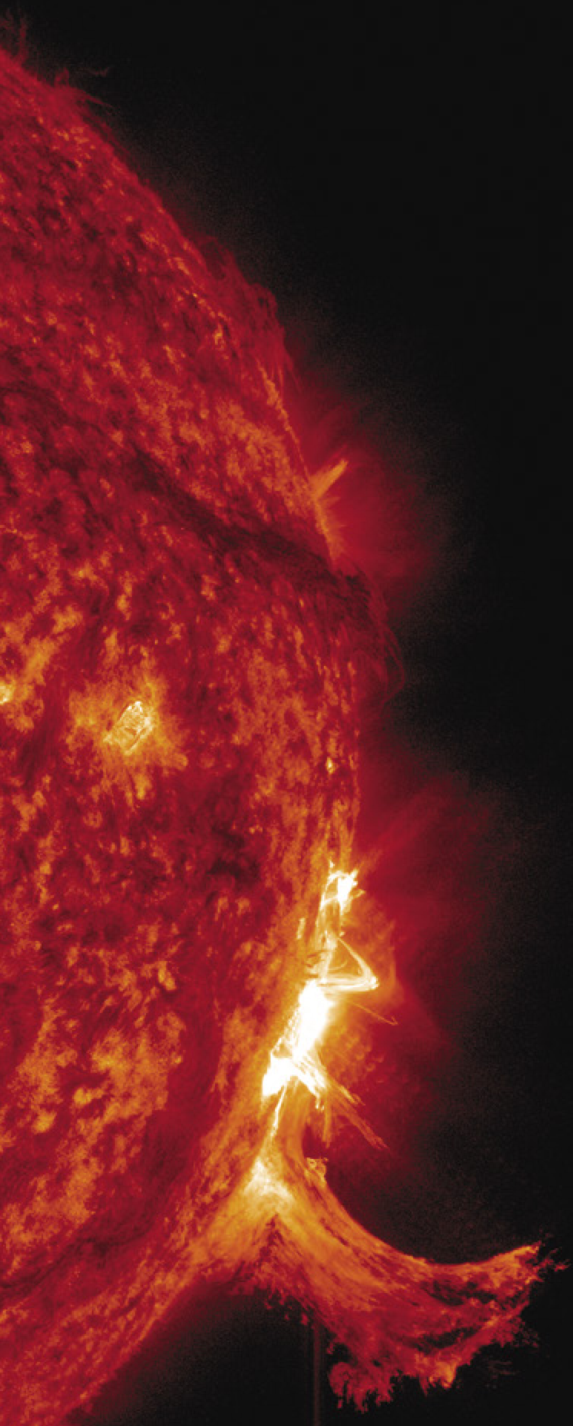


SOLAR FLARE: Plasma bursts from the sun during a 2014 eruption captured by NASA's Solar Dynamics Observatory.



ASTRONOMY

THE SECRET LIFE OF THE SUN

Our closest star has a much more exciting biography than scientists once assumed. New research illuminates the sun's past and potential future

By Rebecca Boyle

Rebecca Boyle is an award-winning freelance journalist based in St. Louis, Mo. She is a contributing writer for the *Atlantic,* and her work regularly appears in *New Scientist, Wired, Popular Science* and other publications and has been anthologized in the *Best American Science and Nature Writing* series.

IN THE BEGINNING,

there was nothing but cold and dark between the atoms that became the solar system. No sun existed 4.6 billion years ago, only a gossamer cloud of remains from earlier stars, stocked with elements forged in previous cataclysms beyond our comprehension. And then something happened.

Maybe a passing celestial nomad's gravity nudged the cloud; maybe a more distant star exploded, loosing a wind that ruffled the atoms, just as a breeze can push leaves into a pile. In any event, the atoms gathered together and began to condense, until finally the material grew hot enough to begin fusing hydrogen into helium. The sun was born, and, not long afterward, so was Earth. Less than a billion years after that, the first life arose, at least on this planet—and now here we are.

This basic story is what science has told for decades: solar birth, a boring stretch of time and then genesis. But powerful new space telescopes and the burgeoning field of "cosmochemistry," as well as genealogy techniques borrowed from biology, are enabling astronomers to write a much richer and more complex biography for the sun. Today scientists know our star was not always solitary. It once had siblings, and it may have even adopted one of their planets. The sun and its planets had, for lack of a less anthropomorphic word, a mother: a giant star whose short life provided

IN BRIEF

Astronomers once thought the sun was an unremarkable star with an unremarkable life story.

Recently, though, scientists have found that the sun had a "mother," "aunts" and "uncles"—and a cadre of "siblings" as well. It may have even stolen a planet from one of its relatives.

And its family tree may live on. When sunlike stars die, astronomers have found, they have a chance to "birth" future stars.

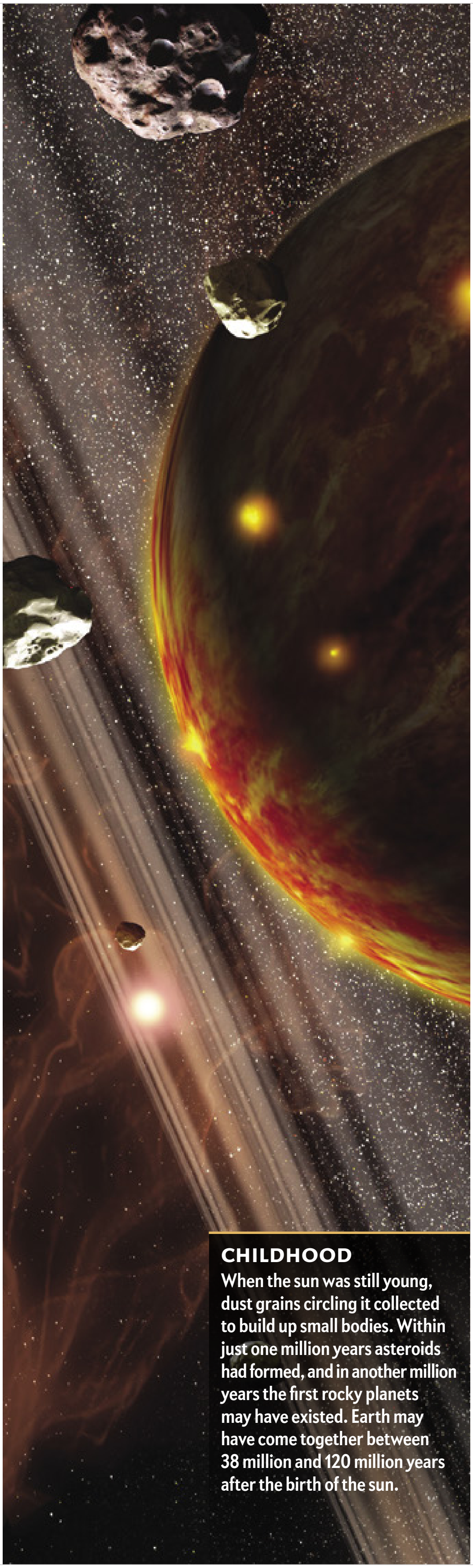
PRECEDING PAGES: NASA'S SOLAR DYNAMICS OBSERVATORY AND AIA, EVE AND HMI SCIENCE TEAMS

The Sun's Life in Chapters

ANCESTORS
The sun may have had a "mother" star that was born a few tens of millions of years before it and died in a supernova explosion (*shown here*) that seeded space with heavy and radioactive elements. Some of these ended up in the sun and the planets of the solar system. In a 2012 study, astronomers named this star "Coatlicue" after the Aztec mother of the sun.

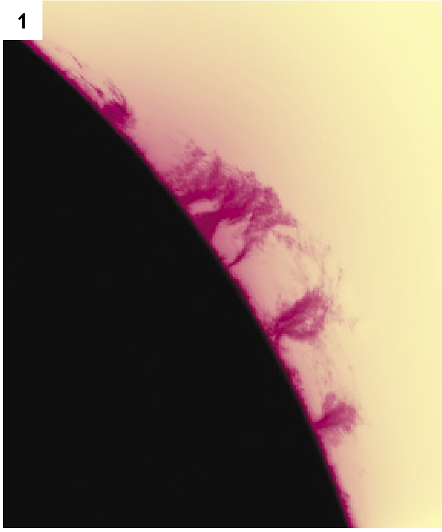
Illustration by Ron Miller

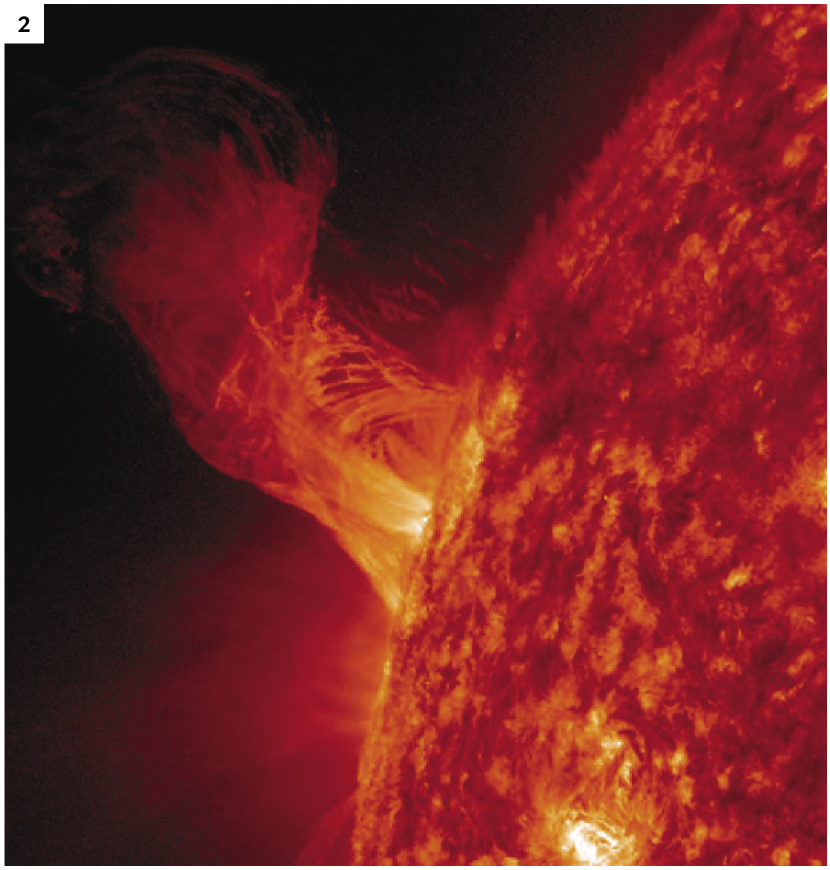
SIBLINGS
The sun was born in a cloud of gas and dust, when enough matter condensed to ignite nuclear fusion. This cloud probably birthed between a few hundred and tens of thousands of other stars that became the sun's littermates (*pictured here*). Over time these stars have drifted apart, but researchers recently identified a candidate for at least one of the sun's siblings.



CHILDHOOD
When the sun was still young, dust grains circling it collected to build up small bodies. Within just one million years asteroids had formed, and in another million years the first rocky planets may have existed. Earth may have come together between 38 million and 120 million years after the birth of the sun.

DEATH
In another five billion years the sun will come to the end of its life. It will very likely lose hold of its outer gaseous layers, which will puff out to form a glowing planetary nebula. At the center, the remains of the sun's core will turn into a small, dense "white dwarf" star. At this point, Earth and the inner planets will be gone (engulfed during the sun's later years), but outer solar system asteroids such as the Kuiper belt objects (*pictured at bottom*) will endure.





SOLAR PROMINENCES rise from the sun's face in these photographs from 2013 (*1*) and 2012 (*2*). The eruptions extend about 30,000 and 160,000 miles from the sun's surface, respectively.

the embryonic material for the solar system. This precursor material might have been isolated from the rest of the galaxy for at least 30 million years, a lengthy gestation that belies the speed at which the sun made planets.

Even the sun's eventual death is coming into new relief. Astronomers know that in about five billion years, it will burn through its hydrogen supply and begin to cool, ballooning into a swollen behemoth whose outer edges might swallow our planet. But they are still learning how the sun's death rattle will influence the interstellar medium (the gas and dust that fills the space between stars), the makeup of future stars and the galaxy as a whole. It is possible that, in death, the sun will become a "mother" itself, enabling new stars and possibly new planets to form.

And in learning more about the sun's past, present and future, scientists are doing more than just writing our own history. The universe may have innumerable stars, but we can know only one intimately. Every insight we glean casts light on the many distant orbs that we will never come to understand so well.

BEFORE THE SUN: SOLAR ANCESTORS

MILLIONS OF YEARS before the sun ignited, before it was a glimmer in the eye of the Milky Way, its ancestors dominated the galactic neighborhood. These earlier stars were themselves the many-times-great-grandkids of the galaxy's first stars, and their generation numbered in the tens of thousands. Within a few million years of their own formation, some of them began to die. Their violent deaths seeded the galactic region with its first heavy elements, such as iron and aluminum. The remnants of these stars gave rise to later generations of stars, including the forebears of the sun.

Astronomers are reconstructing this history using meteorites, leftover crumbs from the birth of the solar system. Researchers compare the amounts of various radioactive isotopes in the meteorites with those in the galaxy's interstellar medium, which is constantly replenished by celestial death throes. The differing abundance of these radioactive materials, which diminish over specific timescales, serves as a clock for astronomers seeking to determine when the solar system's building blocks were finally present.

By following one radioisotope, aluminum 26, Matthieu Gounelle of the French National Museum of Natural History and Georges Meynet of the Geneva Observatory traced the sun's family tree back three generations. Aluminum 26 is radioactive, with a half-life of about 730,000 years—meaning half of any given sample will decay over that time. It is found in meteorites dating to the earliest days of the solar system, and many astronomers assume it originated in a supernova that could have exploded near the sun when it was forming. But a supernova to mark the occasion of the solar system's birth would have been an unusual coincidence. Instead in 2012 and later Gounelle and Meynet showed that the aluminum 26 could have formed inside a massive star.

This star would have been the most massive in our cosmic corner, about 30 times the mass of the sun, according to Gounelle and Meynet's calculations. Like other gargantuan stars, it would have lived a short but spectacular life, exploding a few million years after it ignited. It would have not only synthesized the aluminum 26 but also, in its violent death by supernova, streamed hydrogen gas, heavy metals and radioactive elements into the cloud of gas that would become the solar system. The researchers named this star "Coatlicue," for the mother of the sun in Aztec cosmogony.

Research has provided further clues about how the solar sys-

ALAN FRIEDMAN (1); NASA'S SOLAR DYNAMICS OBSERVATORY AND AIA, EVE AND HMI SCIENCE TEAMS (2) tem's building blocks came to be. In 2014, for instance, scientists in Australia showed that some of the heavy metals, such as gold, silver and platinum on Earth and in meteorites, arrived in the neighborhood some 100 million years before the birth of the sun. A portion of the rare earth elements, such as neodymium, arrived in the sun's gestational environment some 30 million years before it formed. The sun therefore incubated for a lengthy period, with an upper limit of 30 million years.

Although astronomers cannot travel back in time to verify this story, they can compare it against other planetary systems with similar chemical compositions, says Megan Bedell, an astrophysicist at the Flatiron Institute in New York City. And the time line appears consistent. "We are putting the sun in context with its neighbors and seeing that it is a pretty typical star for its formation conditions," she says.

In addition to tracking the sun's forebears, scientists are also using tools from biology to look for its cousins, uncles and other relatives—its broader family tree. Whereas a botanist might use DNA or inherited traits to relate one species of plant to another, astronomers study the ratios of chemical elements in different stars to investigate the relations among them. Didier Fraix-Burnet, an astronomer now at the Institute of Planetology and Astrophysics of Grenoble in France, was one of the first to propose this technique in 2001. He dubbed it "astrocladistics," after cladistics, a term biologists use to describe the technique of mapping inherited traits. Last year Paula Jofré of Diego Portales University in Chile and her colleagues used this method to construct a stellar evolutionary tree for the sun's neighborhood.

Working with a University of Cambridge biologist, Jofré's team used a clustering approach from biology called the distance method, which constructs an evolutionary tree where different branches indicate evolutionary change. In astronomy, the branches represent star populations that are separate in age and movement patterns through the galaxy. Imagine two generations of stars. The first generation has two stars—one large and one small. The more massive star will explode earlier and give rise to a second-generation star in the same way that Coatlicue died and birthed the sun. "The second generation is carrying information from the first generation. They are kind of 'genetically' connected," Jofré says. "So you might be finding a star and its uncle."

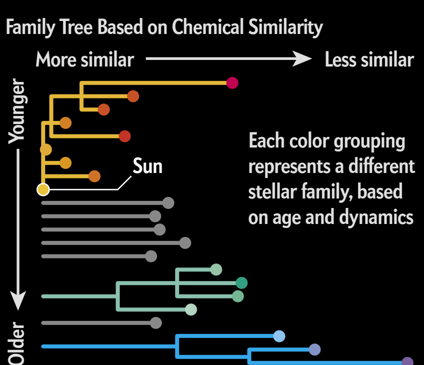
Jofré and her colleagues scrutinized 22 nearby stars similar to the sun and focused on 17 chemical elements as a stand-in for DNA to determine "family" relations. Their analysis grouped the stars by elemental ratio and sorted them into two well-known families of stars. They also found some that belong to a new, previously unknown third group, which Jofré says is still mystifying.

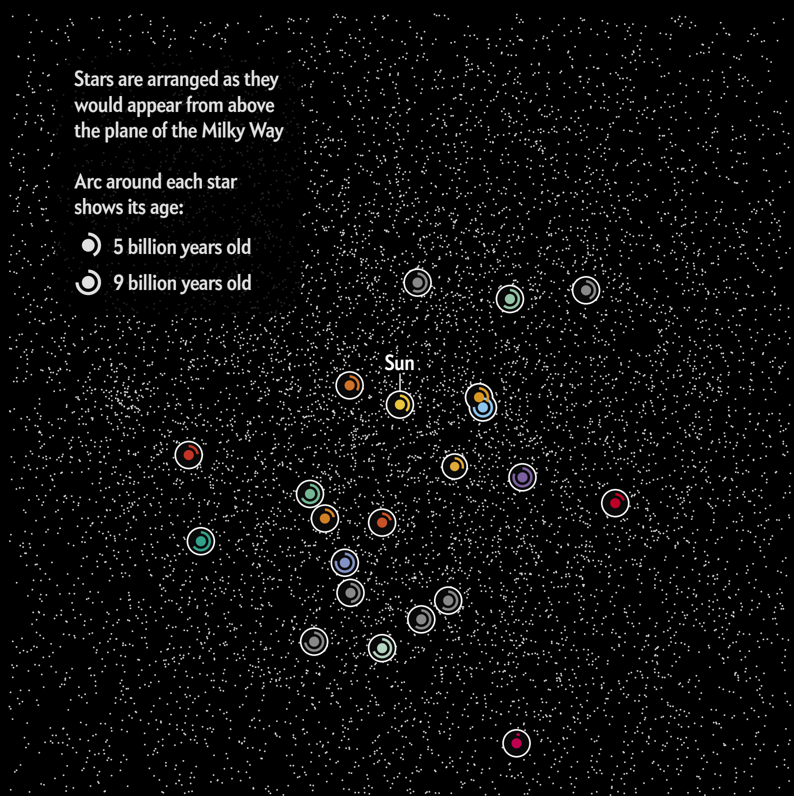
A STAR AND ITS SIBLINGS ARE BORN

FROM THE BIRTH of Coatlicue and its forebears a few tens of millions of years before the sun formed, things stayed busy in the sun's natal cloud. Gas collapsed and ignited, forming other stars. As they switched on, pressure from their stellar winds and the light they emitted would have pushed nearby gas outward, eventually triggering the birth of even more stars: the sun and its littermates. Estimates of the number of those littermates range from a few hundred to tens of thousands. The truth is probably on the lower end,

Local Families

Inspired by biology, astronomer Paula Jofré and her colleagues developed a family tree for our corner of the galaxy. They began with 21 stars that were akin to our sun in color and brightness and analyzed chemical similarities to find relations among them. The scientists found three distinct family groups, each perhaps born of different stellar "parents," whose deaths seeded space with material for the next generation. The sun's group is shown in oranges and reds; gray stars did not fall into any family.





SOURCES: "COSMIC PHYLOGENY: RECONSTRUCTING THE CHEMICAL HISTORY OF THE SOLAR NEIGHBOURHOOD WITH AN EVOLUTIONARY TREE," BY PAULA JOFRÉ ET AL., IN *MONTHLY NOTICES OF THE ROYAL ASTRONOMICAL SOCIETY,* VOL. 467, NO. 1; MAY 11, 2017; HIPPARCOS CATALOGUE. EUROPEAN SPACE AGENCY, 1997

Graphic by Katie Peek

given the fairly stable alignment of the sun's planets: closer siblings would have perturbed the solar system, altering the number and position of planets inside it.

Although they were born relatively close together, the sun's siblings have long since moved on. Over the eons some blew apart into oblivion, and others drifted apart because of minor differences in the speed with which they rotate around the center of the galaxy. Their current positions are all but impossible to match up with their place of origin. "Much like me and my twin brother, we formed together, but we completely dispersed and did separate things," says Keith Hawkins, an astronomer at Columbia University. He says chemical tagging, also known as cosmochemistry—such as the technique of comparing the ratios of certain heavy and light elements in stars—allows scientists to see connections between stars that would otherwise be invisible.

In 2014 Iván Ramírez went looking for the sun's littermates and found one. Now a professor at Tacoma Community College, Ramírez started with about 30 candidates, which he chose based on their chemical compositions and the speeds and directions that they travel through the Milky Way. After further analysis of these characteristics, he narrowed the field to just one star, called HD 162826. It is about 15 percent more massive than the sun and just a bit bluer, he says. Although the sun and its sibling would have formed close together, today HD 162826 is 110 light-years away in the constellation Hercules. It is visible with a decent pair of low-power binoculars, above Hercules' shoulder and not far from the bright star Vega.

Ramírez says his search was partly born of pure interest, but he also wanted to test strategies that he and others will use when they download a gargantuan galactic data set from the new Gaia satellite. The spacecraft is designed to measure stars' brightness and precise position in the sky and will track a billion stars to produce the most detailed 3-D map ever made of the Milky Way. Its latest batch of data, released in April, includes precise measurements for more than 1.3 billion stars. This number is more than an order of magnitude greater than the previous best data set.

Ramírez thinks Gaia will help astronomers find about half of the sun's lost littermates. In doing so, the survey could tell astronomers about the sun's birth environment and its path since then through the Milky Way. The sun is orbiting the galactic center today at roughly 125 miles per second, and astronomers think it has made at least 20 trips around the galaxy so far.

ACTIVE REGIONS ON THE SUN, where magnetic fields churn, form sunspots, shown here in white. The largest of these could fit several Earths inside it. A large detached prominence flies out toward the bottom of the image.

ALAN FRIEDMAN

CHILDHOOD: CREATION OF THE PLANETS

NOT LONG AFTER the sun and its siblings ignited, dust grains around many—if not all—of those stars began coalescing into planets. In our solar system, at least, planet building happened posthaste. Evidence from meteorites suggests that once solid matter condensed, it took less than one million years to form the first generation of asteroids. Largely driven by the decay of aluminum 26, chunks of rock heated up and differentiated into bodies with a metal core and a silicate mantle. Larger rocky worlds were not far behind. Mars may have formed within two million years, according to one estimate. Earth came together between 38 million and 120 million years after the sun did.

Around that time, our star may have captured a planet from a sibling. The putative Planet Nine, a theoretical giant body that astronomers think lurks at the outer edges of the solar system, may be a cousin world, adopted by the sun 100 million years after our star's birth. For such a scenario to have taken place, Planet Nine would have had to orbit its original star at a wide distance, roughly 100 to 500 times the stretch between Earth and the sun (100 to 500 astronomical units). At the same time, this star would have had to swing by the sun, its sibling, at roughly 1,500 times that distance. This type of stellar encounter happens relatively frequently in other star clusters, so astronomers know it is feasible. If Neptune-size planets are common, then many stars are likely to host Planet Nine–type worlds in highly eccentric orbits that make them vulnerable to kidnapping by other stars.

In 2016 Alexander Mustill and Melvyn Davies, both at Lund University in Sweden, and Sean Raymond of the University of Bordeaux in France calculated that the sun could have had several opportunities to snag Planet Nine. It is even possible that the sun grabbed the world without disturbing the Kuiper belt, the ring of comets and asteroids at the solar system's edge.

Planet Nine, a theoretical giant body that astronomers think lurks at the edges of the solar system, may be a cousin world adopted by the sun.

Further study of the solar system's outer objects will help theorists figure out Planet Nine's parentage—if the rumored planet in fact exists. And if it does, it may not be the only interloper from another star to have jostled or joined the sun's family. In 2015 Eric Mamajek, then at the University of Rochester, and his colleagues showed that 70,000 years ago—when modern humans were spreading out from Africa and when the Neandertals still lived—a star called Scholz's star entered the Oort cloud, the spherical shell of icy planetesimals that surrounds the sun beyond the orbit of Pluto. This star approached less than one light-year from the sun—a glancing blow that reshaped the trajectory of some Oort cloud objects, according to a 2018 study led by Carlos de la Fuente Marcos of the Complutense University of Madrid. Nowadays the star is almost 20 light-years away. And astronomers know that smaller foreign bodies can sometimes pay a visit, too. Last fall the sun briefly welcomed the first known voyager from beyond: the interstellar asteroid 1I, or 'Oumuamua. The errant rock was traveling too fast to join the sun's coterie for good, however.

While the sun was forming planets, it was also changing itself. Bedell, who has spent years trying to tease apart the relation between a star's chemical composition and its history of planet making, examined a set of solar twin stars, which are not necessarily from the same birth family but whose chemical compositions match our sun's precisely.

Compared with other stars, Bedell and her colleagues found, the sun is slightly unusual in one key way: it has less rocky material in its exterior layers than do other stars similar to it, and the amount is roughly equivalent to a few Earth masses. One interpretation is that this material "got locked up in terrestrial planets or gas giant cores and is now missing from the outside of the sun," she says. If that is true, then the process of forming planets transformed the sun, just as giving birth changes the bodies of human women.

The revelation may also provide a new way to search for exoplanets. If astronomers find that other sunlike stars have a slightly lower abundance of dusty material, they may be able to deduce that planets surround them, too, Bedell says.

IN THE END

ONE DAY IN ABOUT FIVE BILLION YEARS, the sun will run out of hydrogen fuel in its core. It will mushroom from its current middling size and yellowish color into a red giant, and it will engulf the nearest two, three or maybe four planets. Earth will likely be near, if not within, the aged sun's surface. The sun's core will start to cool, and its nuclear furnace will slowly fade out. As it bloats farther into the solar system, its gravitational field will not be able to hold onto its gigantic, diffuse outer layers. Its atmosphere will float away.

"The sun will become this beautiful planetary nebula, with a white dwarf as its core," Hawkins says. The white dwarf—a small, dense mass containing the sun's remnants—will cool over time, and it will sail through the galaxy for untold eons into the future.

Could the sun then start a new family? In 2016 Hans Van Winckel and Michel Hillen, both at KU Leuven in Belgium, showed that sunlike stars could potentially make a new batch of planets in their old age. Using the Very Large Telescope on a mountaintop in Chile's Atacama Desert, they spotted a hot disk of dust around an old, dying star. It resembled a protoplanetary disk of the kind that swaddles natal stars. This means that some stars—and maybe even the sun—may get a second chance at creating worlds. This scenario, however, would be more likely in binary systems, and our star stands alone.

When the sun dies, what remains will eventually disperse into the interstellar medium, where it will be unlikely to run into enough other material to condense into a new star, Bedell says. "It's more poetic to say it will diffuse out and become part of the next generation, the circle of life and all that," she says. But the sun will probably die "a quiet death in the semiouter region of the galaxy." Little will be left to tell the tale of the adventurous life it lived.

In the meantime, though, we are here. Everything we learn about the sun is not only a truth about our own corner of the cosmos but a window into the many stars we cannot study up close. "I've heard people say in the past that stars in general are a solved problem," Bedell says. "But there is still a lot that we don't understand." Slowly but surely, the sun is helping to change that. SA

MORE TO EXPLORE

Solar System Genealogy Revealed by Extinct Short-Lived Radionuclides in Meteorites. M. Gounelle and G. Meynet in *Astronomy & Astrophysics,* Vol. 545, Article No. A4; September 2012.

Elemental Abundances of Solar Sibling Candidates. I. Ramírez et al. in *Astrophysical Journal,* Vol. 787, No. 2, Article No. 154; June 1, 2014.

FROM OUR ARCHIVES

On the Probable Origin and Age of the Sun. James Croll; August 25, 1877.

The Great Solar Eclipse of 2017. Jay M. Pasachoff; August 2017.

scientificamerican.com/magazine/sa

NEUROSCIENCE

CAN YOU SUPER-CHARGE YOUR BABY?

Hundreds of toys promise to help babies read, learn, do math and walk earlier than expected—many without scientific backing

By Erik Vance

Photo Illustration by Dan Saelinger

WHEN SETH POLLAK'S SON WAS A YEAR OLD, HE AND HIS WIFE,

Jenny Saffran, took a trip to the Babies "R" Us store near their home in Madison, Wis. They wanted to buy a teething ring—nothing special, just a frozen band to numb the baby's gums. Passing through the bears and bicycles, they found the correct display. They pulled a pricey package off the shelf, which read, "Promotes oral motor and language development."

The couple had never heard of such a claim, although it sounded important. Typical parents—worried about their child falling behind—might have bought the product without thinking. But Pollak and Saffran are not typical parents. "My wife is one of the world's leading experts in language development, and we are both Ph.D.s in developmental psychology," Pollak explains. "We are looking at this, and we're like, 'What the hell? How in the world does chewing on a cold thing promote language?'"

There is little evidence to say it does. And the claim is just one example of the disconnect between the research and marketing of child development.

Every parent wants his or her baby to have an early jump on life. Shouldn't toys be part of that? If your baby plays with the right gizmos during the right developmental window, the sales pitch goes, she or he could become smarter, more coordinated and more successful than other babies.

But the very idea that the purpose of a toy is to give your baby an edge "fundamentally misunderstands what's happening in development," says Alison Gopnik, a columnist and leading child psychologist at the University of California, Berkeley. Even if experts could devise such products, "we would have defeated the whole point of childhood," which, she asserts, is for the child to build himself or herself.

Whether it is a black-and-white mobile that supposedly catches a baby's eye or a caterpillar that teaches your toddler to code, American toys that promote child development are rampant. But do they work? Gopnik, along with many developmental psychologists, believes that there is a gaping hole between products and research. Too often toys come with claims based on either questionable science or none at all.

Yet the North American educational toy market is estimated at more than $4 billion in 2018 and is growing rapidly, according to research firm Technavio. Experts say that is because of a deep insecurity in American parents. Has their daughter breastfed too long? Not long enough? Is their son in the right preschool? If babies are not crawling, walking, talking, reading and even doing math early, then they are doing it late.

"Kids are surrounded by a panicked, kind of fearful culture. 'Oh, my God, you're falling behind,'" says Barbara Sarnecka, a cognitive scientist at the University of California, Irvine, who studies language and math acquisition.

Although scientists are fervently trying to understand how the human brain develops and how to help babies and toddlers who are truly developmentally or socially lagging, many toy makers seem to suggest you can supercharge the average kid. Are there any findings that might support these claims?

IN BRIEF

So-called educational toys make myriad claims about helping babies read, learn, do math and walk early, but little science backs them up.

Even if babies do make early advances, research fails to show that a jump leads to any long-term advantages.

Fast-paced video and TV imagery can hamper a baby's ability to understand the pace of the world, leading to attentional problems.

The greatest benefit from play comes from interacting with another human being—so parents should set aside time and be present.

EARLIER IS NOT BETTER

MARKETING TO PARENTS' anxieties begins the moment sperm meets egg. Expectant mothers must carefully manage nutrition, vitamins and stress for fear that any mistakes might have lasting effects on their children. And of course, your fetus needs the proper music.

That's right: the fast track to a prized life starts with music in the womb. There are a number of products that come with speakers that attach to a woman's belly to play music. One gadget, Babypod, goes a step further: it is a bulb-shaped silicone speaker that is inserted inside the woman's vagina. The product site says, "Our initial hypothesis suggests that music ... activates the brain circuits that stimulate language and communication. In other words, learning begins in utero."

It is true that babies learn while in the womb and that music is enriching to young children. But there is no evidence that music enriches a fetus. The creators of Babypod published a paper in the British Medical Ultrasound Society's journal *Ultrasound* showing that fetuses reacted more strongly to their product than to external speakers, but it did not conclude that the reactions were positive or that this strategy translated into smarter children.

"I know of nothing out there that says that this stimulation does anything for your baby," says Kathy Hirsh-Pasek, a developmental psychologist at Temple University and president of the International Congress of Infant Studies. Babypod did not respond to numerous requests for comment.

Hirsh-Pasek specializes in language acquisition in babies, which is a huge research area and a rich target for claims. She says she displays her least favorite toys marketed to anxious parents on a wall in her office.

Speaking is perhaps a baby's most important milestone and is tied to later cognition and working memory. Studies show that babies and young children have certain age windows during which these abilities blossom. Some evidence suggests that how quickly babies learn new words predicts later proclivity; loquacious children tend to be loquacious in later childhood, too.

But is earlier always better? Scientists have tried to tie early speaking to intelligence for decades. A 1982 study based in Ohio found early talkers often had higher IQs later in life. Interestingly, however, the effect disappeared when researchers controlled for cognitive problems and socioeconomic status. This insight, Hirsh-Pasek says, is the crux. Speaking early or late does not determine success; zip code does. Poverty, food instability and violence create stress, and stress delays speech and leads to academic disparity down the line. In many stressful homes, infants simply are not spoken to enough and thus suffer from a language gap that turns into a pervasive performance gap. Yet many toy makers turn this situation into an unfounded assumption: because lack of speech creates a deficit, extra speech will pay dividends.

Sarnecka says that is "just a fantasy—a fantasy that's profitable." Mental stimulation for young children is like vitamins—enough is important, but more is not better. Yet thousands of apps are available. And the average 18-month-old has at least seven DVDs.

"You think you've seen the worst, you know, and then something else hits the market," Hirsh-Pasek says. "One of my all-time favorites, of course, is Your Baby Can Read. To which I answer, 'No, she cannot.'"

Your Baby Can Read was a series of flash cards, videos and books that purported to teach children from three months to five years to read. The product was created by a researcher named Robert Titzer, who claimed to have taught his two daughters to read when they were babies. Conventional studies indicate babies simply cannot understand the written word. Yet the company selling the product offered impressive-sounding, though unpublished, studies and charts, alongside glowing testimonials, including one about a preschooler reading Harry Potter books.

Hirsh-Pasek was not the only one who noticed the aggressive advertising. The Federal Trade Commission, which polices claims, opened two cases involving Titzer, charging that companies he worked with were engaged in deceptive practices.

FTC lawyers reached out to Susan Neuman of New York University to learn more. Neuman is an expert in language acquisition. She had run a randomized controlled study comparing 61 babies who were exposed to Your Baby Can Read against 56 who were not and published the results in the *Journal of Educational Psychology*. Based on 14 measures, such as speech processing, word learning, letter recognition and reading with meaning, she found no difference between the two groups. Well, almost none. Although the children using the program did not advance beyond the others, their parents were convinced they had.

Titzer, for his part, told me he was never involved in marketing decisions and would never have suggested toddlers can read Harry Potter books. But he defends his product and says Neuman did not use it correctly and asked inappropriate questions to test the babies' learning.

In the end, Titzer and the companies settled with the FTC in 2014 for $800,000. The FTC also promised much larger fines should he make similar claims again. He now runs Infant Learning Company, which sells a set of DVDs, printed cards and books called Your Baby Can Learn! The company also sells a kit called Your Child Can Read!

As for the marketing, Titzer says it has changed: "We have babies *looking* at books. Everyone recommends that babies look at books, so I don't see anything wrong with babies looking at books."

Dozens of studies indicate that many video learning programs fail to show reliable results. Titzer insists that his products are measurably superior and notes that he is working on a publication that vindicates them. According to FTC lawyer Annette Soberats, who spoke with a colleague who was involved in the Your Baby Can Read case, her agency considers the matter closed.

FLASH CARDS + VIDEOS = MATH SKILLS

OF COURSE, toys do not exist in a vacuum. There is some pressure from consumers to make sure toys are educational, especially for the very young, says Clement Chau, an expert in child development and a director for toy company LeapFrog Enterprises. "I think there is a tendency to say, 'I want my kid to go to Harvard, so I'm going to buy them a toy from LeapFrog, and they will go to Harvard eventually,'" he says. That viewpoint may be unrealistic, but toys can still be an integrated part of learning, Chau adds.

In the end, it is not clear that parents can supercharge their baby to boost his or her long-term

Erik Vance is a science writer and relatively new father. His first book, *Suggestible You* (National Geographic, 2016), is about how belief affects the brain.

abilities. At least, that is what David Barner says. And he should know; he tried like crazy to supercharge his daughter.

Barner is an expert in the development of math education for children. He knows that math learning is important for cognition and life skills. So he wanted his two-year-old daughter to be a math whiz. He was never great at math himself—both he and his wife preferred reading—but he saw its value. So for months he spent time each day quizzing his child using products that utilize flash cards, videos, games and comic books to teach math to toddlers and preschoolers.

In the end, although he delighted in watching a young mind absorb math in real time, that is pretty much all he got, while his daughter developed a distaste for math. Her true passion and skill? Reading, of course.

Speaking with his professional hat on, Barner thinks parents have less impact on their kids than "things like who your friends are, what school you go to, whether you have access to good resources." Many analyses, such as an ongoing University of Minnesota study with separated twins, also show that personality and proclivities are surprisingly heritable.

Barner's work has revealed that many kids between three and five who can count and even seem to do simple addition do not actually comprehend the principles of numbers but use memorized tricks to get the right answers. Although U.S. toddlers are intensely trained to count, they are quickly passed in math skills by children in places such as Asia.

GOING FOR GOLD

NOT ALL PARENTS want their little darling to win a Fields Medal for mathematics. Some prefer Olympic gold. For that result, they look to motor learning.

"If my baby walked at 10 months instead of 13 months, are they on a fast track to travel-team soccer?" asks Karen Adolph, a child psychologist at New York University. "Does speeding up motor skills have long-term effects?"

Compared with language or math skills, the motor-learning field is small, and many basic questions are still wide open. But a few insights seem clear. The first is, surprisingly, that you can supercharge your baby's ability to sit, crawl and even walk. In 1935 developmental psychologist Myrtle McGraw famously trained one baby to swim, climb and roller skate while his twin brother sat in a crib. But as soon as McGraw allowed the other brother to play as well, he quickly caught up. "Practicing motor skills accelerates motor skills in the short term," Adolph says. But there is "no evidence that it does anything for the long term."

If you want to raise the next Usain Bolt or Nolan Ryan, early walking or throwing probably will not matter. Such skills may, however, offer some cognitive advantages; kids who can sit up can reach for things sooner, and those who walk can explore their world earlier.

Adolph says there is another key difference between movement and cognition: the parents she meets in the laboratory are far less worked up about motor learning in their babies, which corresponds to the toy market as well. No one is selling Your Baby Can Backflip. Some products, such as little pushcarts and walkers, promise to help babies learn to walk, but the marketing statements about that seem muted and secondary to just having fun. If you give a baby a rattle, she or he will learn to shake it. Is that the first step to becoming the drummer in a Rush revival band? No.

Adolph points to running cultures such as the Tarahumara people of Mexico; they begin running at a young age, but they do not walk or crawl especially early. She is now working in Tajikistan, where babies are bound for most of the day. The practice delays when they first walk, but her early evidence shows no differences compared with how Western babies walk by preschool age.

LEARN GRAVITY FIRST

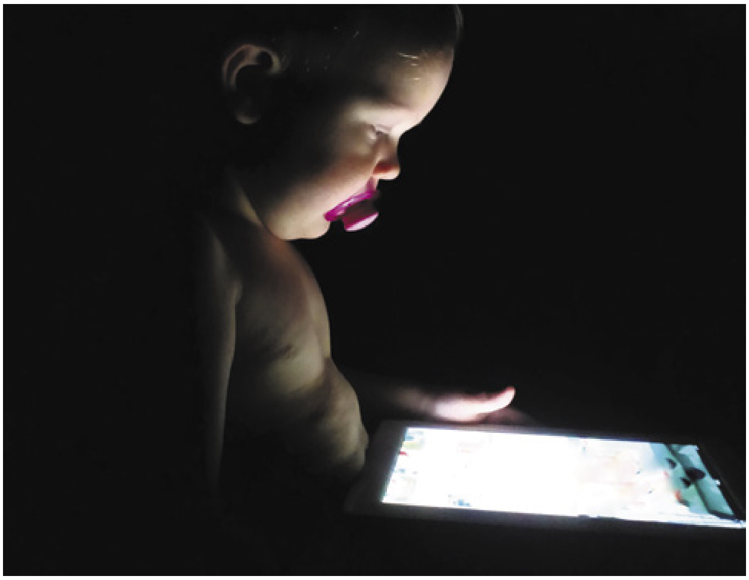
SCIENCE-BASED INVESTIGATIONS indicate that parents cannot supercharge their babies. But that does not mean science has not generated advice for what babies should play with.

Play is incredibly important for developing minds. Just as food nourishes the body, play promotes language, cognition, spatial reasoning and other talents in ways scientists are still trying to understand. And like food, sometimes the simplest options can be the best.

For instance, blocks and Legos pop up often in the scientific literature. Kids who build stuff have better spatial reasoning and, in one controversial study, better math skills. According to experts, there is nothing magical about building; children simply benefit from toys such as balls, dump trucks and ramps that teach them about the physics of gravity, shape and movement. Watching a baby careen toward the floor or into a closed door is terrifying, but these are just their physics experiments to understand how gravity operates and whether two objects can occupy the same space.

Perhaps the most crucial experiments deal with the most enigmatic of phenomena: time. It turns out that babies do not understand time any better than they do gravity or inertia. And some experts worry that if this learning is disrupted, a skewed view can have long-lasting effects.

Dimitri Christakis is a child psychologist at the University of Washington, who directs a children's center at Seattle Children's Hospital. He studies the effect of video screen time on children, which is crucial as children increasingly use tablets, phones and laptops. He has found that it is not the screen that causes problems but the pace of the programming on



MATHIAS DARMELL *Getty Images*; SOURCES: *GLOBAL EDUCATIONAL TOYS MARKET 2017–2021.* TECHNAVIO, JULY 2017 (*markets*); "SCREEN MEDIA AND LANGUAGE DEVELOPMENT IN INFANTS AND TODDLERS: AN ECOLOGICAL PERSPECTIVE," BY DEBORAH L. LINEBARGER AND SARAH E. VAALA, IN *DEVELOPMENTAL REVIEW*, VOL. 30, NO. 2; JUNE 2010 (*DVDs*)

$4 BILLION

North American educational toy market

$2.8 BILLION

Global education apps market for ages 0–4

7+

DVDs owned by the average 18-month-old

it. Games and cartoons that speed up the action or quickly switch scenes may affect a child's "internal metronome," a mechanism that Christakis believes develops in the first three years to help individuals understand the pace of the world. If that pace is set too fast, it can lead to attentional problems—a theory backed by studies in which he has induced deficits in cognition and attention in mice.

Christakis compares older TV shows such as *Mister Rogers' Neighborhood* with modern, frenetic cartoons or video products for infants such as those put out in the past by a company called Baby Einstein. He is concerned that not only are TV and video games faster today but their consumers are younger. Hirsh-Pasek agrees. Her lab has also shown that no matter how interactive a game or show seems to be, it is not as beneficial as a live human being—either in person or via a video phone call. The key for nutritious play is another human who interacts at a normal pace.

Chau, the LeapFrog director, agrees that videos should not replace human interaction but says they can be a part of a child's development. Rather than playing with a real wedge or lever, a baby might do it on a screen while she is not interacting with real people.

But Christakis worries screens could have lasting detrimental effects. By looking at how parts of the brain used glutamate, a basic neurotransmitter involved in learning and memory, he has found connections to cocaine addiction in his attention-challenged mice. Overstimulation led to more enjoyment of cocaine, less sensitization to it and ever more hyperactivity. This is not to say that the same is true in humans or that overstimulated kids will turn to drugs, but addiction relies on reward networks in the brain and habit formation. To better understand these ideas, Christakis is now studying screen addiction in children as young as two years old. That would have been unheard of a decade ago, and he says he has found it in almost 10 percent of his subjects.

"My fear is that we are going to see that go up and that we'll see it start at a younger and younger age as more and more infants and toddlers spend time" on screens, Christakis says. "These devices have a lot of addictive features."

Hidden danger can lurk behind certain products, it seems. But even if educational products aimed at babies may do no harm, there is a dearth of evidence that they convey benefits in the long term. If you simply must buy some cool toy, perhaps find one that *you* want to play with. Because experts agree the time a baby spends with you—hearing you talk and watching you interact with the world—is the best education she can get.

Which brings us back to Pollak and Saffran. Standing in front of the teething ring display, they had to decide whether to try to increase their son's oral motor development. They burst out laughing and put the ring back.

"We went to the grocery store, and we bought him a package of frozen bagels for 99 cents," Pollak says. "I took one out of the freezer and let him chomp on that. It numbed his gums a little bit, and he stopped crying." SA

MORE TO EXPLORE

Becoming Brilliant: What Science Tells Us about Raising Successful Children. Roberta Michnick Golinkoff and Kathy Hirsh-Pasek. American Psychological Association, 2016.

The Gardener and the Carpenter: What the New Science of Child Development Tells Us about the Relationship between Parents and Children. Alison Gopnik. Farrar, Straus and Giroux, 2016.

Gwen Dewar's blog Parenting for the Science-Minded: **www.parentingscience.com**

FROM OUR ARCHIVES

How Babies Think. Alison Gopnik; July 2010.

scientificamerican.com/magazine/sa

A PAINFUL MYSTERY

HEALTH

Endometriosis spreads like a vine through the bodies of roughly 176 million women worldwide, causing agony and infertility. Science has struggled to understand the condition, but new research is sparking hope for improved treatments soon

By Jena Pincott

Illustration by Katherine Streeter

Jena Pincott is a freelance writer who focuses on the quirky, hidden side of science. She is author of several books, including *Do Chocolate Lovers Have Sweeter Babies? The Surprising Science of Pregnancy* (Free Press, 2011). Her writing has appeared in the *Wall Street Journal,* Oprah.com, *Psychology Today* and *Nautilus,* among other publications.

EVERY WOMAN WITH ENDOMETRIOSIS has an origin story, a memory of the first time she knew the pain in her pelvis could not be normal. For Emma, it goes back to the day in 10th-grade history class when she blacked out. The sensation, she says, was how a pumpkin might feel when its insides are scraped. Her gynecologist assumed she was having bad period cramps and gave her birth-control pills. They helped but not enough. "He made me feel as if I were acting a little crazy," says Emma, now in her late 30s, who asked to go by a pseudonym. "It struck me much later that when a woman's medical problem isn't clear-cut, she just isn't believed." Not until about six years after the blackout did she find a doctor who recommended laparoscopic surgery of her abdomen to look for the cause of the pain. That is when she learned she had endometriosis, a disorder in which tissue normally found in the uterine lining, called the endometrium, escapes and takes root in other parts of the body. By then, the disease had carpeted her pelvic organs like kudzu.

In describing endometriosis, ecological comparisons seem apt. Just as the creeping kudzu vine wraps itself around trees and shrubs, smothering anything in its path, so, too, do adhesions (scar tissue) that form when wayward endometrial cells land where they are not supposed to. These adhesions can engulf or bind the bladder, the intestines, the ureter tubes leading

IN BRIEF

Endometriosis afflicts approximately 10 percent of women worldwide, yet it continues to present a medical mystery.

Scientists do not understand why the cells lining the uterus sometimes grow in other places in the body, triggering extreme pain, inflammation and scar tissue.

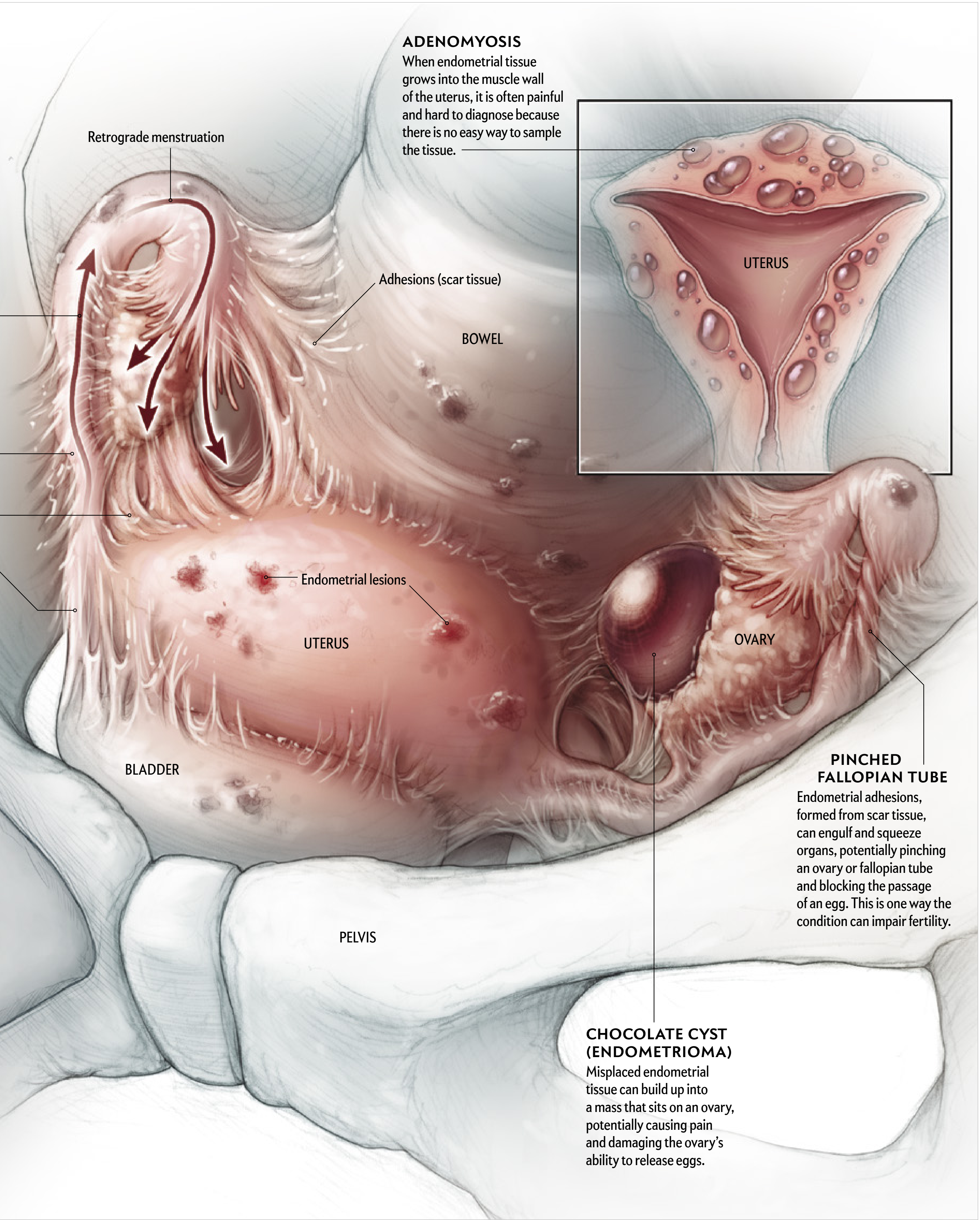
The disorder has long been dismissed and underfunded, but endometriosis is gaining visibility. Research is picking up, leading patients to hope for better treatments soon.

Invasion of Pain

Endometriosis is an agonizing disorder that affects about 10 percent of women worldwide yet largely baffles scientists. It occurs when endometrial cells, which normally line the walls of the uterus, escape and grow elsewhere, prompting inflammation and scar tissue.

RETROGRADE MENSTRUATION

A leading theory suggests that endometriosis occurs when menstrual fluid during a woman's period flows backward through the fallopian tubes into a woman's abdomen. Wherever it lands, the endometrium continues to grow and shed with the woman's cycle, and the trapped blood and tissue lead to scarring and inflammation.



Illustrations by David Cheney

to the kidneys and other pelvic organs. Lesions that are surgically removed often grow back: more than half of women who have them cut out return for another operation within seven years. When surgeons go in, they might see the bowels, ovaries and sciatic nerve bound in a macramé of scar tissue or a fallopian tube squeezed so tightly that an egg cannot pass through.

Despite the manifest damage it can cause, endometriosis is a mystery. Doctors know that it runs in families and is linked with several genetic variants—heritability hovers around 50 percent—but genes cannot yet explain its occurrence or predict its path. The degree of scarring and the number and location of lesions have little to do with the severity of the symptoms, which, besides pain, can include heavy bleeding, discomfort during sex and bowel movements, and often devastating infertility. Some patients find relief in surgery and drugs, whereas others, even with few lesions, try every known remedy and still live in constant pain.

For decades endometriosis has been ignored, and research into it has been underfunded. Endometrial pain and other symptoms reduce women's productivity at work by nearly 11 hours a week—7 percent of a 40-hour work week—according to results released in 2011 from the Global Study of Women's Health, which surveyed more than 1,400 women in 10 countries.

Finally, patient advocacy, social media activism and women-led movements for social change have started to bring attention to the problem, and the medical community has begun to reckon with its history of underestimating and undertreating women's health issues. Researchers are developing tools to study the complicated origins of endometriosis, to diagnose it and to design targeted treatments. Yet even at a time when women are raising their voices for better care, too many remain undiagnosed and in pain.

THE INVASION CONUNDRUM

"FIRST, HOW DOES THE TISSUE get outside the uterus?" asks Linda G. Griffith, a professor of biological and mechanical engineering at the Massachusetts Institute of Technology. As scientific director of the M.I.T. Center for Gynepathology Research and an endometriosis patient herself, she is deeply vested in the question, which has perplexed her fellow scientists for decades. No one knows for certain how or why endometrial cells show up outside the endometrium.

The prevailing theory, called retrograde menstruation, was proposed nearly a century ago. John Sampson, a gynecologist, observed that menstrual fluid containing cells from the uterus can flow backward up the fallopian tubes. Bits of that fluid, he suggested, stick to pelvic organs and the abdominal lining or float in pelvic fluid and spread to distant sites. It happens to just about every woman and is normally cleared by the immune system. But sometimes, Sampson's theory goes, the cells implant wherever they land. The misplaced tissue acts as if it is still in the uterus: it sprouts hormone receptors and responds to hormonal signals. Every month it grows as the uterine lining grows, secreting hormones, and sheds when the cycle ends. But unlike a period, the blood and tissue get trapped in the pelvis and trigger inflammation. Over time the inflammation leads to scarring and adhesions.

Ever since Sampson, researchers have been divided about the underlying cause of the disease. Is the defect in the "seed," the rogue endometrial cells, or is it in the "soil," the abdominal environment where those cells implant and spread? Theories on the seed side blame defective endometrial cells or stem cells. The soil side claims that endometriosis is primarily an immune dysfunction. A third theory splits the difference, saying, essentially, that the soil changes the seed. "Women with endometriosis may have had normal endometrial cells until the lesions took root and created changes in the tissue," Griffith explains, suggesting that the immune response to the lesions is the likely driver. The resulting inflammation may alter the expression of progesterone and estrogen receptors in endometrial cells: as a result, cells pump out more estradiol, a form of estrogen that fuels growth of lesions, unchecked by progesterone. In a baboon experiment in 2006, researchers were able to induce endometriosis by injecting normal uterine lining into the pelvic cavity.

Kevin G. Osteen, a professor of obstetrics and gynecology at Vanderbilt University, has proposed that environmental toxins play a role, at least in some cases. His research focuses on one of the most toxic of environmental pollutants, the industrial byproduct dioxin, and dioxinlike chemicals called polychlorinated biphenyls (PCBs), which are found in meat, fish, dairy products and, in varying amounts, all our bodies. Osteen's theory is that exposure to these toxins in utero disrupts the physiology of the developing endometrium. When he and his colleagues exposed human endometrial tissue to dioxin in a series of experiments, the tissue became resistant to progesterone and prone to inflammation. Without progesterone to tamp down enzymes known as matrix metalloproteinases, which regulate the monthly rebuilding of the uterine lining, endometrial tissue may become invasive, spreading beyond its normal domain in the uterus.

Griffith suspects that whatever caused her endometriosis, it happened early in life. Retrograde menstruation may apply to many cases, she says, but probably not hers. She developed harrowing symptoms from day one of her first period, long before lesions from menstruation had time to develop. Some researchers argue that patients in this category may have had a retrograde flow of endometrial cells during the normal vaginal bleeding that often occurs shortly after birth in female infants. Or when baby girls are still in the womb, endometrial-like cells or stem cells could have landed outside the uterus, sometimes as far afield as the lungs and brain (evidence of these wandering cells has been found in miscarried and aborted fetuses). "Those cells could sit there until the girl starts going through puberty," Griffith explains—like ticking time bombs.

Similar to cancer, endometriosis has many causes and manifestations. As Griffith puts it, "It's likely not one disease but many."

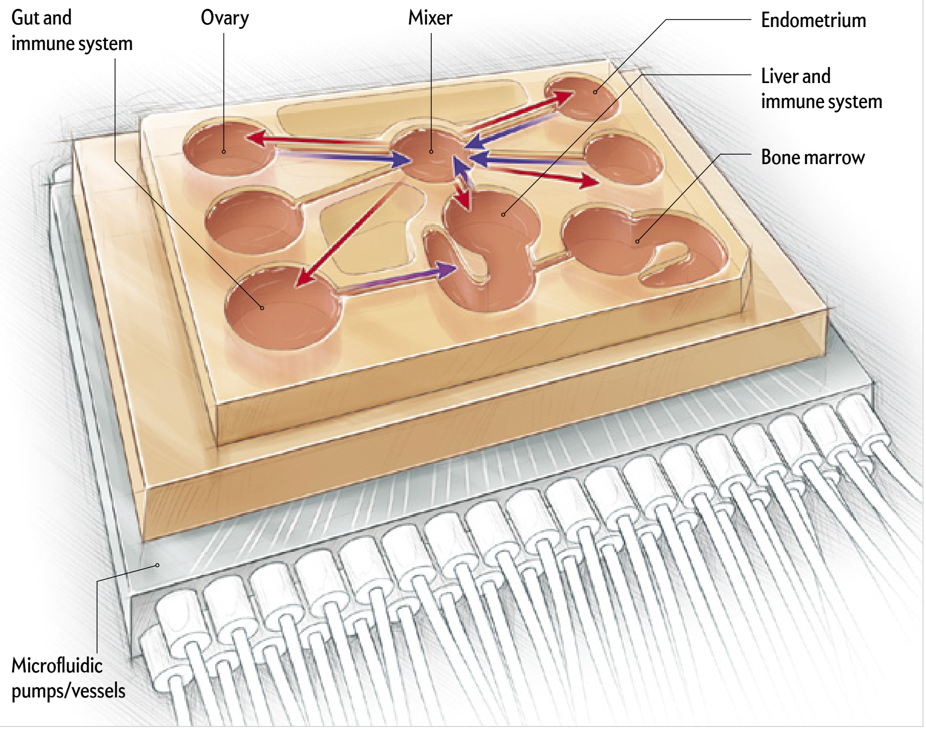
AN ECOSYSTEM OF PAIN

WHEN WOMEN TALK about endometriosis, they talk about pain. They talk about the sick days from school or work, lost time and opportunities, the diminishment of life's pleasures. They talk about arranging their calendar around their period or a night on morphine in the ER. One of the hardest things for them to hear is that the pain is "all in their head."

Female suffering has a history of being downplayed by the medical establishment. In 2008 a study in the journal *Academic Emergency Medicine* found that women wait longer than men in emergency rooms before receiving treatment for the same abdominal pain, and they are 13 to 25 percent less likely than their male counterparts to receive opioid painkillers (after controlling for age, race, triage class and pain score). An earlier study of cardiac patients found that nurses were likelier to ad-

Organs on a Chip

Scientists are designing microscale versions of body organs to test drugs to treat endometriosis. These so-called organs-on-a-chip avatars contain real living cells that scientists can expose to hormones, pharmaceuticals and other cues. Each platform contains a set of mini organs important for disease processes, plus a mixing chamber, or "mixer," to simulate systemic circulation. For example, the uterine lining (endometrium) and ovary here are connected to gut, liver and bone marrow, which are involved in drug metabolism and immune response. This PhysioMimetics platform is being developed at the Massachusetts Institute of Technology.



minister painkillers to men and to give women sedatives. And even when women do get painkillers, the medication may be less safe and effective for them because many pain studies have been conducted on men or male mice.

Even after finally getting a diagnosis, Emma lost an ovary to endometriosis when she was 26. A decade later she gave birth to a daughter and is now relatively pain-free but not without regret about the years she spent misdiagnosed and undertreated. "If I could redo my life," she says, "I'd have pushed for answers sooner." She did not know that endometriosis even existed when her pain first started. Nor, it seemed, did her doctors, she says.

One reason doctors and even patients minimize pain caused by endometriosis is that it flares up during menstruation when women are "supposed" to feel bad. "Pain is very subjective. Cramps are the only pain that is considered 'normal,' and it's hard to know when that pain is abnormal," explains Hugh S. Taylor, chair of obstetrics, gynecology and reproductive sciences at the Yale School of Medicine. Taylor adds that social norms have prevented open conversation about menstrual pain, pain during sex or pain with bowel movements—all red flags of endometriosis. "Fortunately," he says, "these barriers are decreasing," and doctors, as well as patients, increasingly feel comfortable bringing these topics up and investigating their causes.

And patients can play a more active role in the fight against endometriosis. For instance, they can participate in research through the "citizen scientist" app Phendo, recently launched by biomedical informatics scientists at Columbia University. Users track and identify their patterns and triggers, and the data will be used to study the disease's causes and to design treatments.

"For decades endometriosis advocates have been cultivating communities that empower, inform and educate patients," says Casey Berna, a patient advocate and organizer. "Now there is a movement to reject historically paternalistic approaches to care and to include the patient voice, especially when managing complex diseases."

In April, Berna and her colleagues organized a protest by patients outside the Washington, D.C., headquarters of the American College of Obstetricians and Gynecologists (ACOG), demanding its member doctors be better trained to diagnose endometriosis and to get patients the best and latest treatments—to stop, for instance, prescribing needless hysterectomies. "To put it plainly," Berna says, "the current standards are responsible for decades of suffering endured by millions of patients. We're calling on the ACOG to work with patient advocates and endometriosis experts to utilize all of their resources to address this crisis of care."

Experts agree that too many physicians still miss the disorder. "Pediatricians and most primary care doctors are [still] not well educated about endometriosis," Taylor says. And when endometriosis goes undiagnosed, it often worsens. "Misplaced endometrial tissue has higher than usual levels of aromatase, an enzyme that makes the lesions estrogen-dominant, which in turn drives their growth," explains Pamela Stratton, a gynecologist and surgeon at the National Institutes of Health. The lesions also become resistant to progesterone, which would otherwise help curb endometrial growth and fight inflammation. As a result, inflammation reigns: prostaglandins (lipids that form more quickly when tissue is damaged) and pro-inflammatory proteins called cytokines act on nerve endings and ratchet up pain sensitivity. Over time adhesions form and interfere with the function of pelvic organs, causing more pain.

One of the strange features of endometriosis pain is that it bears little relation to the severity or location of the lesions. A woman with few lesions may feel as if her pelvic organs are being pulverized in a meat grinder, whereas a serious "stage IV" patient with lumps that protrude from her belly may be pain-free. Doctors may overlook adenomyosis, which occurs when endometrial tissue invades the muscle wall of the uterus; lesions here are difficult to see during surgery, but the patient is in eye-popping agony. For many women pain persists even after lesions have receded or are surgically removed.

At this point, the problem is not just in the pelvis anymore, Stratton explains; now it is a central nervous system disorder. All too often with endometriosis, the brain has been tuned in to pain for so long that it cannot turn off, even after the pain trigger is gone. In this condition, called central sensitization, neural wiring has effectively remodeled itself to be "alert to hurt." Any minor disturbance, including ovulation, menstruation and sex, triggers and perpetuates the pain. Genetics may play a role, Stratton notes, but the details are not well understood. Women with few or tiny lesions can still suffer debilitating chronic pain, leading to central sensitization, she says. A troubling irony is that these women may be the most likely to have a doctor tell them there is nothing wrong because many gynecologists are unaware of the possibility of central sensitization. "Because they are not neuroscientists," Stratton says, "they don't consider what neuroscientists have learned about pain."

Stratton, who straddles both worlds, is exploring treatments to address pain and perhaps reverse central sensitization in endometriosis patients. If a drug can relieve pain for an extended period, she posits, the central nervous system may be able to reset its pain threshold. She is conducting a clinical trial of botulinum toxin, commonly known as Botox. Injected in the pelvic floor, it relaxes muscle spasms and may alter the chemicals involved in pain signaling. Although some clinicians already administer Botox off-label for endometriosis pain, Stratton says, she should know if the treatment works around late 2019, after she has tracked patients for a year.

The stakes are high. Chronic pain causes sleeplessness, anxiety, depression, irritability and brain fog. Several neuroimaging studies have found alterations in the gray matter of chronic pain patients, including loss of volume in the hippocampus (which may explain memory impairment) and the prefrontal cortex (which may underlie deficits in pain regulation and cognitive function). A small study of endometriosis patients with chronic pelvic pain found shrinkage in the thalamus, insula and other regions associated with pain modulation. Tracking chronic back pain patients, researchers at Northwestern University compared the loss in gray matter volume—1.3 cubic centimeters every year—to the effects of 10 to 20 years of normal aging.

A BLIGHT ON FERTILITY

WHEN WOMEN WITH ENDOMETRIOSIS talk about their fears, infertility ranks high. About half of women with infertility have endometriosis. In a cruel trick of nature for those who struggle to conceive, endometriosis pain is said to feel like labor pain. A blockage of the fallopian tube can avert the passage of the egg from the ovary to the uterus, and inflammation from scarring or surgery around the ovaries can compromise egg follicle quality and quantity. Pro-inflammatory cytokines and other elements in the peritoneal fluid surrounding the pelvic organs can reduce sperm motility in the fallopian tubes and damage eggs and embryos. Problems can arise in the hormones, too. Conception is a hormonal and immunological symphony; in endometriosis, the conductor has left the room. Normally after ovulation, the concentration of estrogen receptors in the uterine wall dwindles to prepare for implantation. Progesterone rises, cueing the endometrial lining to receive and nourish the fertilized egg. The hormone calms the uterus and prevents contractions. (The root of progesterone is "progestation.") But in endometriosis, the uterine lining is resistant to progesterone, and the competing hormone estradiol remains dominant, among other factors that make the environment less receptive to a blastocyst. Even if implantation occurs, progesterone resistance may lead to a higher risk of miscarriage and premature birth.

All too often with endometriosis, the brain has been tuned in to pain for so long that it cannot turn off, even after the pain trigger is gone.

Adding to the complexity are clues that the endometrium has a microbiome, which also becomes disordered in endometriosis. Recent studies suggest that *Lactobacillus* bacteria dominate the uterus in most women and have a part in implantation and support of the growing embryo. The idea remains speculative, but chronic inflammation caused by endometriosis may kill off lactobacilli, creating a microbial imbalance in the uterus that perpetuates inflammation and potential infertility. In 2016 a preliminary investigation published in the *American Journal of Obstetrics & Gynecology* found that when non-*Lactobacillus* microbes dominate, as they do in endometriosis, implantation occurred at only one third the normal rate, and the number of miscarriages shot up. Although the cause of the connection is not clear, studies such as this one have inspired research into the role of the endometrial microbiome in endometriosis, and some doctors may consider testing endometrial cultures before fertility treatment.

There are success stories, too. Approximately 43 to 55 percent of endometriosis patients are able to conceive through one cycle of in vitro fertilization (IVF), depending on the stage of their disease, and women with endometriosis who do become pregnant through IVF have similar live birth rates to those without the disease. In the hormonal milieu of pregnancy, symptoms usually subside. Breastfeeding, too, is linked with a lower risk of endometriosis. This 2017 finding, derived from a data set of more than 70,000 women, showed that for every three months of exclusive breastfeeding, the risk of a woman developing endometriosis drops by 14 percent, compared with breastfeeding for less than a month. It remains an open question whether lactation-related hormones and immunological factors can relieve the symptoms of women who already have endometriosis.

BETTER TOOLS AND TREATMENTS

WHEN SCIENTISTS TALK about endometriosis, they always bring up the seven-year hitch: the average lapse between the onset of pain and a diagnosis, by which time a lot of damage may be done. A diagnosis currently requires a surgical procedure (laparoscopy), but the disease could be caught much earlier if it could be identified with a simple blood, saliva or urine test. The challenge is to find the right signal to look for.

In recent years several laboratories have homed in on microRNAs (miRNAs): short, noncoding sequences of RNA that regulate gene expression and are shed by tissues. In 2016 Taylor's group identified three miRNAs that are more prevalent in endometriosis patients, compared with control subjects. Taylor's company, DotLab, will use these miRNAs as a basis for the first diagnostic saliva test for endometriosis, which Taylor says has an accuracy of well over 90 percent. The test, administered by prescription, is poised to launch later this year. If it succeeds, women may receive treatment earlier, Taylor says, and doctors may also use it to discern whether a drug they prescribe is effective. After all, a diagnosis, early or not, does not ensure relief. Some drugs work at first, then lose effectiveness. Others trigger menopauselike symptoms.

In the future, a newly diagnosed patient might start her treatment with a skin biopsy, envisions Julie Kim, a professor of obstetrics and gynecology at Northwestern University. Cells gathered from a tiny skin punch in a woman's thigh or lower hip would be engineered to travel backward in developmental time to become induced pluripotent stem (iPS) cells, which can grow into any cell in the body: endometrial cells, liver cells, kidney cells, and so on. Each cell type would be used to seed a "micro organ" on a tablet-sized electric circuit that represents her body—in other words, her medical avatar.

Several organ-on-a-chip avatars are already here. The one Kim built as co-investigator resides at the Woodruff Lab at Northwestern and has a name: the EVATAR (a mash-up of "Eve" and "avatar"). It is a miniature female reproductive system, complete with micro ovaries, fallopian tube, uterus, cervix and liver. Like other patient avatar platforms, the EVATAR's "organs" are harbored in dime-sized vessels that sit on a plate connected to a computer. Artificial blood flows through micro channels that connect the organs, carrying hormones, nutrients, and growth and immune factors between organs. The EVATAR has a monthly cycle but does not bleed.

A patient with an EVATAR would know which drugs are likeliest to help her; after all, every micro organ on the platform holds her specific genetic blueprint. "Say we're testing a drug designed to reduce endometrial lesions," proposes Kim, describing the kind of study she anticipates doing with the EVATAR. Her lab would expose the system to the experimental treatment. During the menstrual cycle, the scientists would collect and analyze data from each organ to see, at the cellular level, if the drug is safe and effective against that patient's lesions. This kind of experiment also avoids the problem of many drugs and treatments being tested on men and animals and then not translating to women and opens the door to custom medicine.

Kim's lab has shown a proof of concept with the EVATAR, but developing an endometriosis platform and testing drugs could take up to five years, Kim says. It may be longer before the platform can test individual patients; the time line depends on many factors involved in taking a research tool to the clinic. The project can only work, she says, "if the resources are available and there is a priority given to endometriosis research."

In Griffith's view, custom drug testing on individual patient avatars is prohibitively expensive, but organs on a chip still have a role to play in figuring endometriosis out. Instead of using an organ-on-a-chip platform for each patient, Griffith hopes to classify women with endometriosis by several molecular markers, similar to what is done for breast cancer, then develop drugs that target each type. "All patients are different," she says, "but we believe there may be groups of patients with common features."

The first step toward finding those groups, Griffith explains, is to build computer disease models and a few hypothetical classification schemes. Next, she would recruit hundreds of patients from multiple clinics and test those models on them. Griffith predicts that three to five groups will emerge that have different types of dysfunction, each with characteristic molecular signatures.

Griffith's organ-on-a-chip platform—called PhysioMimetics—can connect up to 10 mini-organ systems on an integrated circuit, including a tiny endometrium designed by Christi Cook, a former Ph.D. student in Griffith's lab. The chip endometrium consists of a polymer "hydrogel" scaffolding that supports several layers of endometrial tissue cell types. Researchers can apply various hormones and inflammatory cues to the tissues to see what happens.

Once Griffith has identified her disease-type groups—each with its own unique molecular markers—she plans to use the organ-on-a-chip platform and partner with pharmaceutical makers to test drugs that target the specific disease pathways in each group. If the drug appears to be safe and effective on the avatars, she will try it on flesh-and-blood patients.

Despite the promise of organs on a chip and other tools, however, the medical community has a long way to go to fight endometriosis effectively. Funding for research on the disorder is still incommensurate with the disease's societal costs: $62 billion annually in the U.S., including lost work productivity and direct health care costs, according to a 2012 study by the World Endometriosis Research Foundation. An NIH report shows that in the U.S., nearly $1 billion will be spent on diabetes research in 2018, compared with $7 million on endometriosis, which afflicts about the same percentage of women. "If you look in PubMed," the online archive for biomedical studies, Griffith says, "you will find more than 20,000 papers for erectile dysfunction but only about 2,000 papers on adenomyosis, which is estimated to be as common as endometriosis. Who misses work for the first one?"

Fortunately, Griffith says, talent is attracted to the field because the research is "fascinating scientifically"—and also happens to be crucial to society. After all, there is no cure yet: the closest thing is a surgical absence of disease, to which Emma would add, "And a subjective absence of pain." When chronic pain goes away, the mind heals. Gray matter can and does regrow. But like kudzu, endometriosis is tough to subdue—beating it back will take a concerted effort by researchers and doctors, as well as a real financial commitment from a society finally ready to take this disorder seriously. SA

MORE TO EXPLORE

Columbia University's Phendo, an app to track endometriosis: **http://citizenendo.org/phendo**
Endometriosis saliva test from DotLab: **www.dotlab.com**

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ECOLOGY

SHRINKING ANIMALS

A rise in global temperatures may be making all kinds of creatures smaller—a trend with worrisome implications

By Marta Zaraska

Illustration by Marc Burckhardt

Marta Zaraska is a freelance science writer and author of *Meathooked: The History and Science of Our 2.5-Million-Year Obsession with Meat* (Basic Books, 2016). She lives in rural France with her husband, daughter and two old dogs.

THE WORLD GOT HOT IN A HURRY 56 MILLION YEARS AGO. IN JUST 10,000 YEARS—AN EYEBLINK of geologic time—temperatures shot up by as much as eight degrees Celsius, according to paleoclimate data. In one swampy lowland that is now part of Wyoming, the average annual temperature reached about 26 degrees C, similar to the humid tropical coasts of today's Indonesia. One of the locals, loping along in the heat, was a small, brownish animal, with pointy ears and long legs made for running. At roughly four kilograms, the creature was the size of a small dog, perhaps a diminutive terrier. It was, in fact, a horse.

IN BRIEF

Going back millions of years, fossil evidence shows that when the environment heats up, animal body size goes down.

Today, as climate warms, this connection is being seen in fishes, snakes, sheep, butterflies, salamanders and rodents.

Smaller size may be the result of ways that temperature alters animal metabolism, and the changes could affect food supply and world ecosystems.

Ancient horses were not exactly Arabian stallions before the warming: at about 5.5 kilograms, they resembled tiny antelopes. But they shrank considerably once this period, known as the Paleocene-Eocene Thermal Maximum, began. This particular horse, called *Sifrhippus,* went down in body size by a staggering 30 percent. And that was not the end of the downsizing, says Abigail D'Ambrosia Carroll, a graduate student in environmental science at the University of New Hampshire, who studies the fossil remains of the animals. During a later warming phase, 53 million years ago, horse sizes shrank again in many lineages, according to research published in 2017. The bodies of other mammals, such as a rabbit-sized creature that was an ancestor of modern deer, got smaller, too.

This link between shrinking animals and rising temperatures is not just ancient history. Many present-day species are declining in size as the planet warms. Common toads have gotten smaller, as have marine iguanas, snakes, tortoises, salamanders, wood rats, dung flies, butterflies in the Arctic, several kinds of North Sea fishes and a species of sheep. The reason for this pattern has puzzled scientists, but an answer is now emerging from various experiments, as well as field observations and fossils. That answer focuses on energy needs: a smaller, less energy-intensive body may confer survival advantages in warmer surroundings, and therefore animals in hotter areas evolve, over many generations, to become smaller. "I think we are getting closer to understanding these mechanisms," says Janet Gardner, a biologist at the Australian National University in Canberra.

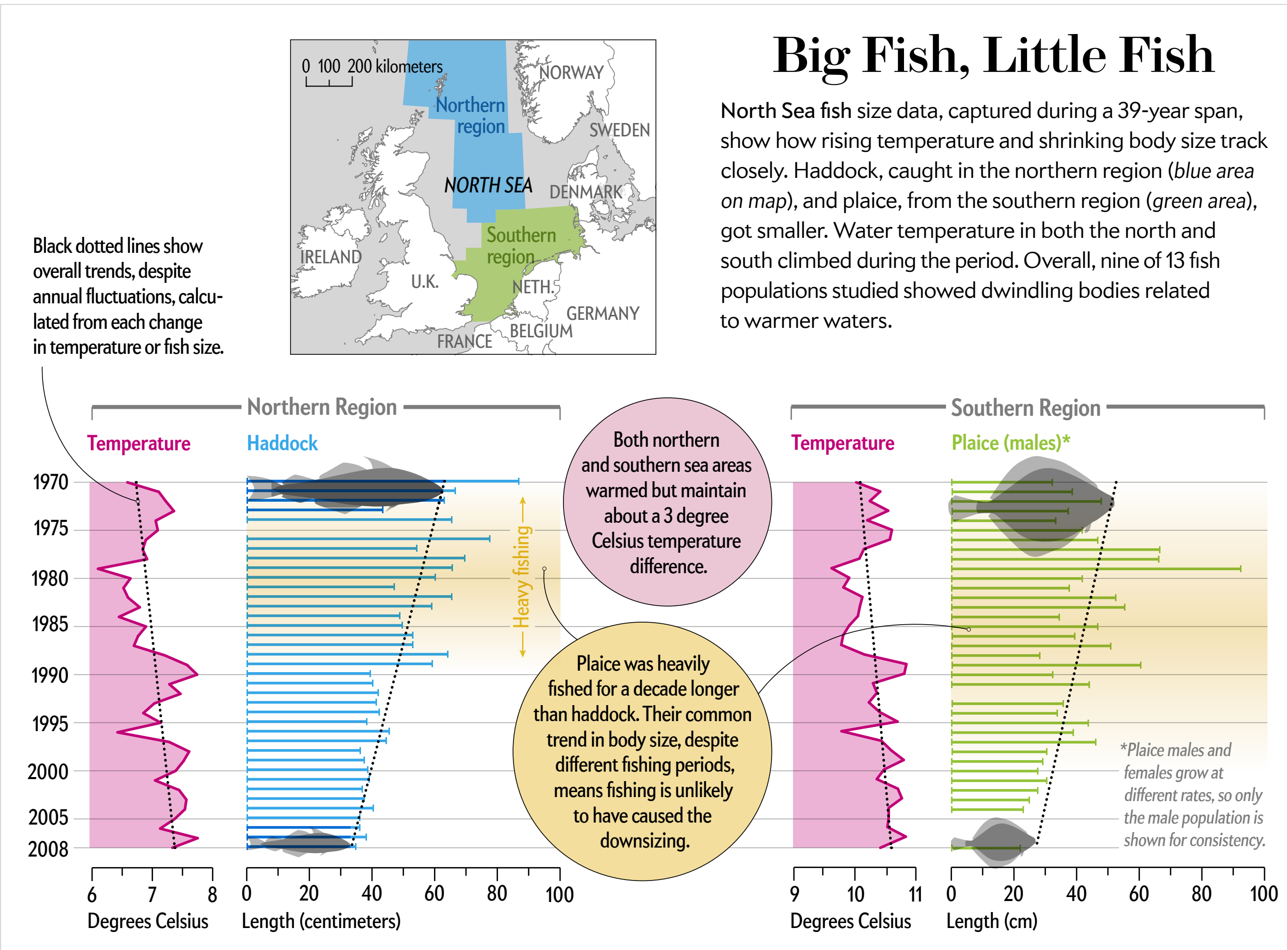
Beyond solving a biological mystery, the growing understanding suggests yet another cause for concern about the effects of climate change. "Smaller sizes could result in extinctions, in the extreme, or disruptions in food webs or other ecosystem-level processes that can directly affect services by animals that benefit humans," says Michael Sears, an evolutionary biologist at Clemson University. One study has suggested that in the next 30 years, we could see significant shrinking of many of the world's fish species. Although the exact degree of the size change is debatable, many scientists agree it could have serious consequences that ripple up the food web.

THE CLIMATE CONNECTION

THE FOSSIL RECORD can get quite detailed when it comes to tracing a strong relation between temperature and body size. One animal that left behind a great amount of data is the bushy-tailed wood rat. The width of wood rats' fecal pellets (droppings) turns out to correlate closely with the size of the individual that excreted them. The pellets also fossilize quite well, creating a long record in sediments that can be analyzed year by year. When scientists at the University of New Mexico and the U.S. Geological Survey went through 25,000 years of fecal pellet data in a study published in 1995, they discovered that wood rat body size fluctuated over that time, going up and down in step with climate changes.

Why would such a connection exist? Back in the 19th century, German biologist Carl Bergmann suggested it might have something to do with a need to regulate body heat. He observed that warm-blooded animals in colder, higher latitudes tend to be larger than mammals that lived closer to the equator and have relatively smaller body-surface-to-weight ratios—there are no slender, giraffelike necks or long, ostrichlike legs near the poles. Bergmann hypothesized that it is easier for a mammal to save body heat if its surface-area-to-volume ratio is smaller rather than bigger. (When people curl up to keep snug in the cold, they are minimizing their surface area.) Yet this idea does not account for the variation now observed in insects, fishes and other nonmammals.

A more complete explanation is emerging from modern laboratory experiments with different kinds of animals: many scientists think the shrinkage may have something to do with changes in animal metabolism



Big Fish, Little Fish

North Sea fish size data, captured during a 39-year span, show how rising temperature and shrinking body size track closely. Haddock, caught in the northern region (*blue area on map*), and plaice, from the southern region (*green area*), got smaller. Water temperature in both the north and south climbed during the period. Overall, nine of 13 fish populations studied showed dwindling bodies related to warmer waters.

SOURCES: ALAN R. BAUDRON (PERSONAL COMMUNICATION); "WARMING TEMPERATURES AND SMALLER BODY SIZES: SYNCHRONOUS CHANGES IN GROWTH OF NORTH SEA FISHES," BY ALAN R. BAUDRON ET AL., IN *GLOBAL CHANGE BIOLOGY*, VOL. 20, NO. 4; APRIL 2014

and in the food needs that go with it. One thing researchers have observed is that when you put the young of many species in warmer environments, the animals grow faster at first but then mature sooner. As a result, individuals end up at a more modest adult size than they would have in cooler surroundings. (Imagine people maturing at the age of eight; we certainly would all be shorter.) In 2012 Andrew Hirst, an evolutionary biologist now at the University of Liverpool in England, and his colleagues published a meta-analysis of experiments on maturation and temperature in 169 species that live on land or in water. They found that 90 percent are mature at smaller body sizes when temperatures are higher. "It's an incredibly widespread phenomenon," Hirst says.

Maturation time is intimately tied to metabolism, which increases when the mercury goes up. Metabolism is a chemical reaction, and "chemical reactions just happen faster at higher temperatures than at lower temperatures," explains Vanessa Messmer, a marine biologist at James Cook University in Queensland. In recent experiments Messmer and her colleagues investigated how metabolism changes with temperature in coral reef fish of different sizes. Their results, published in 2017 in *Global Change Biology,* showed that the maximum metabolic rates in one fish species can increase a whopping 44-fold when the temperature of its water is raised from 28.5 to 33 degrees C. The experiments also demonstrated that small fishes are better at regulating their metabolism in high temperatures than are large fishes, giving a possible survival advantage to the tiny ones.

A faster metabolism means that a creature needs more food, and if an animal cannot get enough nutrition to offset the boost in metabolism, it will have to divide its scarce energy between growth and reproduction. Reproduction usually wins out—it is the survival of the species, after all—and the animals mature and reproduce at a smaller size. And with climate change, it may sometimes simply get too hot to eat. When temperatures get higher than 15 to 20 degrees C, Alpine goats experience such discomfort that they reduce the time spent foraging. Birds actually pant to get rid of excess heat, which makes eating difficult. "You can't forage as efficiently, and you are spending more energy to stay cool than you can actually gain through eating—and adults that lose weight and are in poor condition might produce smaller offspring," Gardner says.

In amphibians such as salamanders, scientists have seen how size reduction could get passed through generations. "Let's say the climate gets warmer in one area of the Appalachian Mountains," says Karen Lips, an en-

Graphic by Amanda Montañez, Map by Mapping Specialists vironmental scientist at the University of Maryland, College Park. "The salamanders living there are now warmer, with higher metabolic rates, and need to eat more to stay at their usual body size. If they can't get enough food in the new climate, they will lose weight. We also know from many studies that smaller amphibians produce fewer offspring—or the same number but smaller offspring. So the animals in a warmer environment will, over time, either get smaller in size, or their population will get smaller."

IF IT ISN'T THE HEAT?

THERE IS, HOWEVER, at least one competing explanation for some shrinking animals, and that is simply that humans are catching and eating the bigger ones. If humans are catching most of the larger fish, for example, that could also remove genes responsible for larger body size from the population. Animals that remain and reproduce would have the genetic makeup for smaller bodies. "By catching larger fish, we humans can create an evolutionary pressure on fish to be smaller," says Alan R. Baudron, an environmental scientist at the University of Aberdeen in Scotland.

Yet Baudron points out that there are holes in the overfishing theory. In a 2014 *Global Change Biology* paper, he and his colleagues showed that over a span of 39 years, beginning in 1970, very different species in the North Sea, such as haddock, herring and plaice, have become smaller. These three species experienced severe fishing pressures at different points. Haddock, for example, was heavily fished in the 1970s and 1980s, whereas plaice was the target of fishing nets through the 1990s as well. Yet body size reductions do not reflect those different periods, a staggered effect one would expect if overfishing a particular population led to smaller fish size. Instead the shrinkage in both species more closely tracks a rise in water temperature. Of 13 fish populations Baudron studied, nine followed this pattern. "If you can still find a common trend in body size across all these species—which is what we *have* found—then it's more likely due to the common factor—that is, temperature—rather than the species-specific fishing pressure," Baudron says. Fishing may play a role in this tale of shrinking fishes, but it is not the dominant factor, he says.

There may be yet other reasons animals get smaller as the planet warms up, and many—like the metabolic changes—are related to energy intake and use. Animals' food may be getting smaller. Warmer winters at the poles may mean easier survival for smaller individuals. If droughts are becoming more common, amphibians may reduce their size to avoid desiccation.

A variety of causes might best explain why animal species are shrinking at different rates. And some are not changing at all or are even getting bigger—that has happened with a few species of migratory birds in the U.S., for example. "There are just so many things that are changing at the same time that it's difficult to predict how every single organism is going to respond," says Jennifer A. Sheridan, an environmental scientist now at Yale-NUS College in Singapore and lead author of a 2011 review on shrinking body sizes. For some animals, it may be easier than it is for others to find enough food to satisfy the increased metabolic needs, she says. For others, the current temperature rise may not be enough to drive a change in metabolism.

Yet the downsizing that has so far been documented does worry many scientists. One 2013 *Nature Climate Change* paper concluded that if the trend of declining body sizes in fishes continues, by 2050 the average maximum body weight of various species may go down by 14 to 24 percent globally. That would mean, among other things, less food to feed a growing human population. Some scientists at the time objected that the model in the study somewhat exaggerated the speed of body size changes, although others felt it was accurate. Baudron believes the research can still "give us an idea of the extent of the problem." For some species, reduced body sizes could also lead to extinctions—it may be better to be smaller in a gradually warming climate, but it is also harder to survive extreme weather. Last but not least, ecosystems can be put out of balance if predators and prey do not change sizes together. "There might be mismatches between something that's shrinking a lot and something that's not shrinking very much," Hirst says.

The fossils do indicate that size changes are not one-way trips. If temperatures decrease, animals could grow larger again. According to climate change predictions, however, humans are unlikely to see that happen. ■

WARMER AND SMALLER: This large adult tooth (*left*) comes from a horse species, *Arenahippus,* that lived about 53.8 million years ago. The smaller tooth (*right*) comes from the same species but 100,000 years later, after climate warmed sharply.

GRACE DELGADO

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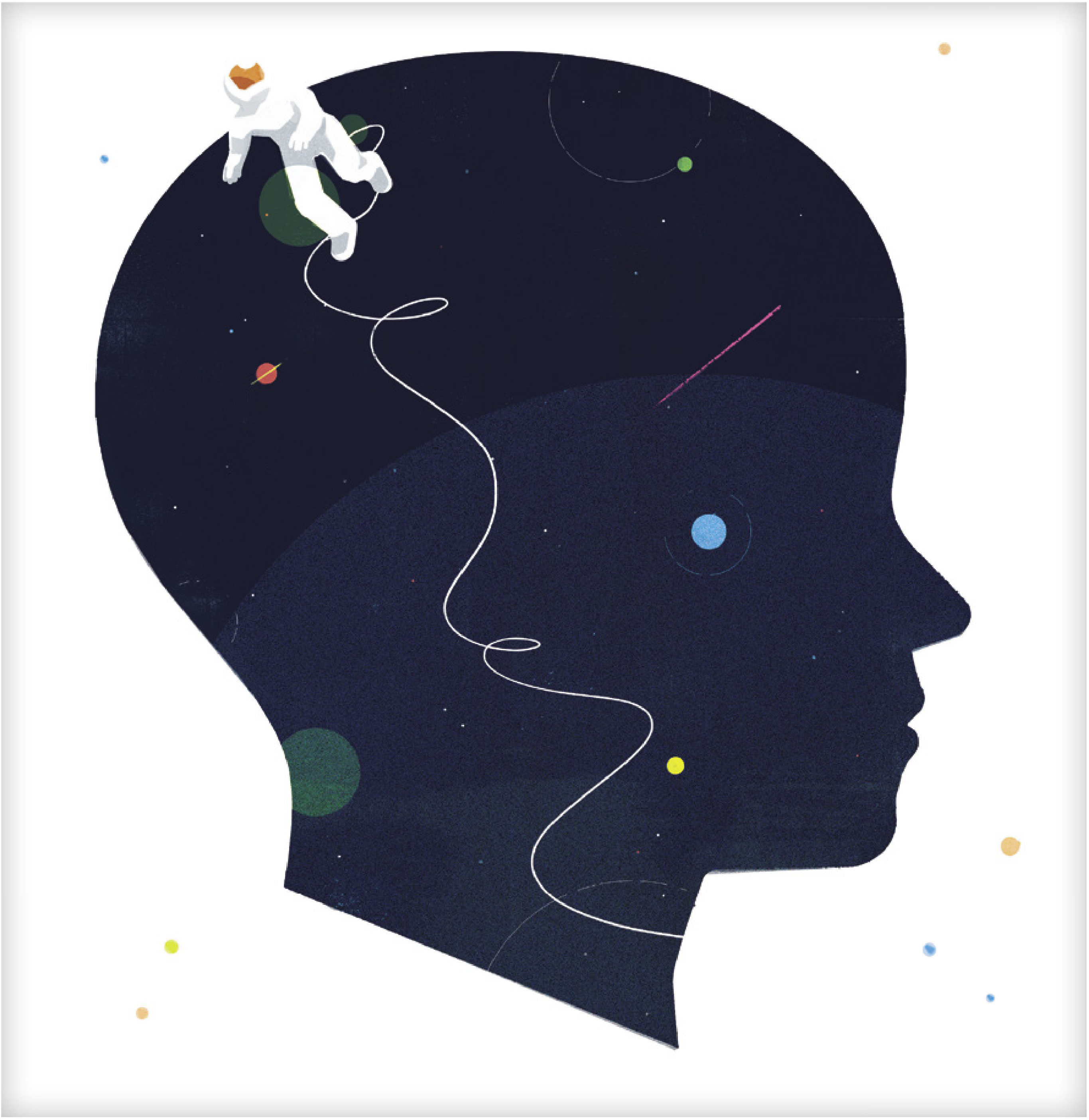
Innovations IN

SPECIAL REPORT FROM nature SCIENTIFIC AMERICAN

THE BIGGEST QUESTIONS IN SCIENCE



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Looking at the Stars

"WE ARE ALL IN THE GUTTER, BUT SOME OF US are looking at the stars," Oscar Wilde wrote. Ever since an early human sat by the glowing embers of a fire on a winter night, as others fell asleep and the camp quietened, we have pondered the mysteries of existence. What are those points of light studding the sky? What are these movements within my belly? Where did this life come from? What is life? How do I protect this being from all harm?

Such questions have occupied not only ordinary humans through the ages but also philosophers and, later, scientists. In recent centuries we have learned so much—and such marvelous things—about the worlds around and within us that it may sometimes seem that no nook is left unexplored, no miracles left for us to unravel. The truth is, though, that every new discovery leads us to ever deeper questions. We know what the stars are, but their motion defies explanation. We can look into the farthest crannies of the universe, but the more we see, the more we suspect that we may never, truly, understand it all. We have a good idea of how the body works, but the mind remains elusive. We know what life is but not where that first spark came from. We can observe unimaginably minute objects, but the more we try to control them, the more they seem to evade our grasp.

This special report on "The Biggest Questions in Science," which is being published in both *Scientific American* and *Nature,* is sponsored by the Kavli Prize. It was produced independently by *Scientific American* and *Nature* editors, who have sole responsibility for all the editorial content. Beyond the choice to sponsor this particular topic, the Kavli Prize had no input about the content of the articles in this package.

Madhusree Mukerjee
Senior Editor

INSIDE

Cover and main illustrations by Chris Gash

QUANTUM GRAVITY

What Is Spacetime?

Physicists believe that at the tiniest scales, space emerges from quanta. What might these building blocks look like?

By George Musser

PEOPLE HAVE ALWAYS TAKEN SPACE FOR GRANTED. It is just emptiness, after all—a backdrop to everything else. Time, likewise, simply ticks on incessantly. But if physicists have learned anything from the long slog to unify their theories, it is that space and time form a system of such staggering complexity that it may defy our most ardent efforts to understand.

Albert Einstein saw what was coming as early as November 1916. A year earlier he had formulated his general theory of relativity, which postulates that gravity is not a force that propagates through space but a feature of spacetime itself. When you throw a ball high into the air, it arcs back to the ground because Earth distorts the spacetime around it, so that the paths of the ball and the ground intersect again. In a letter to a friend, Einstein contemplated the challenge of merging general relativity with his other brainchild, the nascent theory of quantum mechanics. That would not merely distort space but dismantle it. Mathematically, he hardly knew where to begin. "How much have I already plagued myself in this way!" he wrote.

Einstein never got very far. Even today there are almost as many contending ideas for a quantum theory of gravity as scientists working on the topic. The disputes obscure an important truth: the competing approaches all say space is derived from something deeper—an idea that breaks with 2,500 years of scientific and philosophical understanding.

DOWN THE BLACK HOLE

A KITCHEN MAGNET neatly demonstrates the problem that physicists face. It can grip a paper clip against the gravity of the entire Earth. Gravity is weaker than magnetism or than electric or nuclear forces. Whatever quantum effects it has are weaker still. The only tangible evidence that these processes occur at all is the mottled pattern of matter in the very early universe—thought to be caused, in part, by quantum fluctuations of the gravitational field.

Black holes are the best test case for quantum gravity. "It's the closest thing we have to experiments," says Ted Jacobson of the University of Maryland, College Park. He and other theorists study black holes as theoretical fulcrums. What happens when you take equations that work perfectly well under laboratory conditions and extrapolate them to the most extreme conceivable situation? Will some subtle flaw manifest itself?

General relativity predicts that matter falling into a black hole becomes compressed without limit as it approaches the center—a mathematical cul-de-sac called a singularity. Theorists cannot extrapolate the trajectory of an object beyond the singularity; its time line ends there. Even to speak of "there" is problematic because the very spacetime that would define the location of the singularity ceases to exist. Researchers hope that quantum theory could focus a microscope on that point and track what becomes of the material that falls in.

Out at the boundary of the hole, matter is not so compressed, gravity is weaker and, by all rights, the known laws of physics should still hold. Thus, it is all the more perplexing that they do not. The black hole is demarcated by an event horizon, a point of no return: matter that falls in cannot get back out. The descent is irreversible. That is a problem because all known laws of fundamental physics, including those of quantum mechanics as generally understood, are reversible. At least in principle, you should be able to reverse the motion of all the particles and recover what you had.

A very similar conundrum confronted physicists in the late 1800s, when they contemplated the mathematics of a "black body," idealized as a cavity full of electromagnetic radiation. James Clerk Maxwell's theory of electromagnetism predicted that such an object would absorb all the radiation that impinges on it and that it could never come to equilibrium with surrounding matter. "It would absorb an infinite amount of heat from a reservoir maintained at a fixed temperature," explains Rafael Sorkin of the Perimeter Institute for Theoretical Physics in Ontario. In thermal terms, it would effectively have a temperature of absolute zero. This conclusion contradicted observations of real-life black bodies (such as an oven). Following up on work by Max Planck, Einstein showed that a black body can reach thermal equilibrium if radiative energy comes in discrete units, or quanta.

Theoretical physicists have been trying for nearly half a century to achieve an equivalent resolution for black holes. The late Stephen Hawking of the University of Cambridge took a huge step in the mid-1970s, when he applied quantum theory to the radiation field around black holes and showed they have a nonzero temperature. As such, they can not only absorb but also emit energy. Although his analysis brought black holes within the fold of thermodynamics, it deepened the problem of irreversibility. The outgoing radiation emerges from just outside the boundary of the hole and carries no information about the interior. It is random heat energy. If you reversed the process and fed the energy back in, the stuff that had fallen in would not pop out; you would just get more heat. And you cannot imagine that the original stuff is still there, merely trapped inside the hole, because as the hole emits radiation, it shrinks and, according to Hawking's analysis, ultimately disappears.

This problem is called the information paradox because the black hole destroys the information about the infalling particles that would let you rewind their motion. If black hole physics really is reversible, something must carry information back out, and our conception of spacetime may need to change to allow for that.

ATOMS OF SPACETIME

HEAT IS THE RANDOM MOTION of microscopic parts, such as the molecules of a gas. Because black holes can warm up and cool down, it stands to reason that they have parts—or, more generally, a microscopic structure. And because a black hole is just empty space (according to general relativity, infalling matter passes through the horizon but cannot linger), the parts of the black hole must be the parts of space itself. As plain as an expanse of empty space may look, it has enormous latent complexity.

Even theories that set out to preserve a conventional notion of spacetime end up concluding that something lurks behind the feature-less facade. For instance, in the late 1970s Steven Weinberg, now at the University of Texas at Austin, sought to describe gravity in much the same way as the other forces of nature. He still found that spacetime is radically modified on its finest scales.

Physicists initially visualized microscopic space as a mosaic of little chunks of space. If you zoomed in to the Planck scale, an almost inconceivably small size of 10^{-35} meter, they thought you would see something like a chessboard. But that cannot be quite right. For one thing, the grid lines of a chessboard space would privilege some directions over others, creating asymmetries that contradict the special theory of relativity. For example, light of different colors might travel at different speeds—just as in a glass prism, which refracts light into its constituent colors. Whereas effects on small scales are usually hard to see, violations of relativity would actually be fairly obvious.

The thermodynamics of black holes casts further doubt on picturing space as a simple mosaic. By measuring the thermal behavior of any system, you can count its parts, at least in principle. Dump in energy and watch the thermometer. If it shoots up, that energy must be spread out over comparatively few molecules. In effect, you are measuring the entropy of the system, which represents its microscopic complexity.

If you go through this exercise for an ordinary substance, the number of molecules increases with the volume of material. That is as it should be: If you increase the radius of a beach ball by a factor of 10, you will have 1,000 times as many molecules inside it. But if you increase the radius of a black hole by a factor of 10, the inferred number of molecules goes up by only a factor of 100. The number of "molecules" that it is made up of must be proportional not to its volume but to its surface area. The black hole may look three-dimensional, but it behaves as if it were two-dimensional.

This weird effect goes under the name of the holographic principle because it is reminiscent of a hologram, which presents itself to us as a three-dimensional object. On closer examination, however, it turns out to be an image produced by a two-dimensional sheet of film. If the holographic principle counts the microscopic constituents of space and its contents—as physicists widely, though not universally, accept—it must take more to build space than splicing together little pieces of it.

The relation of part to whole is seldom so straightforward, anyway. An H_2O molecule is not just a little piece of water. Consider what liquid water does: it flows, forms droplets, carries ripples and waves, and freezes and boils. An individual H_2O molecule does none of that: those are collective behaviors. Likewise, the building blocks of space need not be spatial. "The atoms of space are not the smallest portions of space," says Daniele Oriti of the Max Planck Institute for Gravitational Physics in Potsdam, Germany. "They are the constituents of space. The geometric properties of space are new, collective, approximate properties of a system made of many such atoms."

What exactly those building blocks are depends on the theory. In loop quantum gravity, they are quanta of volume aggregated by applying quantum principles. In string theory, they are fields akin to those of electromagnetism that live on the surface traced out by a moving strand or loop of energy—the namesake string. In M-theory, which is related to string theory and may underlie it, they are a special type of particle: a membrane shrunk to a point. In causal set theory, they are events related by a web of cause and effect. In the amplituhedron theory and some other approaches, there are no building blocks at all—at least not in any conventional sense.

Although the organizing principles of these theories vary, all strive to uphold some version of the so-called relationalism of 17th- and 18th-century German philosopher Gottfried Leibniz. In broad terms, relationalism holds that space arises from a certain pattern of correlations among objects. In this view, space is a jigsaw puzzle. You start with a big pile of pieces, see how they connect and place them accordingly. If two pieces have similar properties, such as color, they are likely to be nearby; if they differ strongly, you tentatively put them far apart. Physicists commonly express these relations as a network with a certain pattern of connectivity. The relations are dictated by quantum theory or other principles, and the spatial arrangement follows.

Phase transitions are another common theme. If space is assembled, it might be disassembled, too; then its building blocks could organize into something that looks nothing like space. "Just like you have different phases of matter, like ice, water and water vapor, the atoms of space can also reconfigure themselves in different phases," says Thanu Padmanabhan of the Inter-University Center for Astronomy and Astrophysics in India. In this view, black holes may be places where space melts. Known theories break down, but a more general theory would describe what happens in the new phase. Even when space reaches its end, physics carries on.

ENTANGLED WEBS

THE BIG REALIZATION of recent years—and one that has crossed old disciplinary boundaries—is that the relevant relations involve quantum entanglement. An extrapowerful type of correlation, intrinsic to quantum mechanics, entanglement seems to be more primitive than space. For instance, an experimentalist might create two particles that fly off in opposing directions. If they are entangled, they remain coordinated no matter how far apart they may be.

Traditionally when people talked about "quantum" gravity, they were referring to quantum discreteness, quantum fluctuations and almost every other quantum effect in the book—but never quantum entanglement. That changed when black holes forced the issue. Over the lifetime of a black hole, entangled particles fall in, but after the hole evaporates fully, their partners on the outside are left entangled with—nothing. "Hawking should have called it the entanglement problem," says Samir Mathur of Ohio State University.

Even in a vacuum, with no particles around, the electromagnetic and other fields are internally entangled. If you measure a field at two different spots, your readings will jiggle in a random but coordinated way. And if you divide a region in two, the pieces will be correlated, with the degree of correlation depending on the only geometric quantity they have in common: the area of their interface. In 1995 Jacobson argued that entanglement provides a link between the presence of matter and the geometry of spacetime—which is to say, it might explain the law of gravity. "More entanglement implies weaker gravity—that is, stiffer spacetime," he says.

Several approaches to quantum gravity—most of all, string theory—now see entanglement as crucial. String theory applies the holographic principle not just to black holes but also to the universe at large, providing a recipe for how to create space—or at least some of it. For instance, a two-dimensional space could be threaded by fields that, when structured in the right way, generate an additional dimension of space. The original two-dimensional space would serve as the boundary of a more expansive realm, known as the bulk space. And entanglement is what knits the bulk space into a contiguous whole.

In 2009 Mark Van Raamsdonk of the University of British Columbia gave an elegant argument for this process. Suppose the fields at the boundary are not entangled—they form a pair of uncorrelated systems. They correspond to two separate universes, with no way to travel between them. When the systems become entangled, it is as if a tunnel, or wormhole, opens up between those universes, and a spaceship can go from one to the other. As the degree of entanglement increases, the wormhole shrinks in length, drawing the universes together until you would not even speak of them as two universes anymore. "The emergence of a big spacetime is directly tied into the entangling of these field theory degrees of freedom," Van Raamsdonk says. When we observe correlations in the electromagnetic and other fields, they are a residue of the entanglement that binds space together.

Many other features of space, besides its contiguity, may also reflect entanglement. Van Raamsdonk and Brian Swingle, now at the University of Maryland, College Park, argue that the ubiquity of entanglement explains the universality of gravity—that it affects all objects and cannot be screened out. As for black holes, Leonard Susskind of Stanford University and Juan Maldacena of the Institute for Advanced Study in Princeton, N.J., suggest that entanglement between a black hole and the radiation it has emitted creates a wormhole—a back-door entrance into the hole. That may help preserve information and ensure that black hole physics is reversible.

Whereas these string theory ideas work only for specific geometries and reconstruct only a single dimension of space, some researchers have sought to explain how all of space can emerge from scratch. For instance, ChunJun Cao, Spyridon Michalakis and Sean M. Carroll, all at the California Institute of Technology, begin with a minimalist quantum description of a system, formulated with no direct reference to spacetime or even to matter. If it has the right pattern of correlations, the system can be cleaved into component parts that can be identified as different regions of spacetime. In this model, the degree of entanglement defines a notion of spatial distance.

In physics and, more generally, in the natural sciences, space and time are the foundation of all theories. Yet we never see spacetime directly. Rather we infer its existence from our everyday experience. We assume that the most economical account of the phenomena we see is some mechanism that operates within spacetime. But the bottom-line lesson of quantum gravity is that not all phenomena neatly fit within spacetime. Physicists will need to find some new foundational structure, and when they do, they will have completed the revolution that began just more than a century ago with Einstein.

George Musser is a contributing editor for *Scientific American.* He is author of *Spooky Action at a Distance* (2015) and *The Complete Idiot's Guide to String Theory* (2008).

What Is Dark Matter?

An elusive substance that permeates the universe exerts many detectable gravitational influences yet eludes direct detection

By Lisa Randall

Physicists and astronomers have determined that most of the material in the universe is "dark matter"—whose existence we infer from its gravitational effects but not through electromagnetic influences such as we find with ordinary, familiar matter. One of the simplest concepts in physics, dark matter can nonetheless be mystifying because of our human perspective. Each of us has five senses, all of which originate in electromagnetic interactions. Vision, for example, is based on our sensitivity to light: electromagnetic waves that lie within a specific range of frequencies. We can see the matter with which we are familiar because the atoms that make it up emit or absorb light. The electric charges carried by the electrons and protons in atoms are the reason we can see.

Matter is not necessarily composed of atoms, however. Most of it can be made of something entirely distinct. Matter is any material that interacts with gravity as normal matter does—becoming clumped into galaxies and galaxy clusters, for example.

There is no reason that matter must always consist of charged particles. But matter that has no electromagnetic interactions will be invisible to our eyes. So-called dark matter carries no (or as yet undetectably little) electromagnetic charge. No one has seen it directly with his or her eyes or even with sensitive optical instruments. Yet we believe it is out there because of its manifold gravitational influences. These include dark matter's impact on the stars in our galaxy (which revolve at speeds too great for ordinary matter's gravitational force to rein in) and the motions of galaxies in galaxy clusters (again, too fast to be accounted for only by matter that we see); its imprint on the cosmic microwave background radiation left over from the time of the big bang; its influence on the trajec-

tories of visible matter from supernova expansions; the bending of light known as gravitational lensing; and the observation that the visible and invisible matter gets separated in merged galaxy clusters.

Perhaps the most significant sign of the existence of dark matter, however, is our very existence. Despite its invisibility, dark matter has been critical to the evolution of our universe and to the emergence of stars, planets and even life. That is because dark matter carries five times the mass of ordinary matter and, furthermore, does not directly interact with light. Both these properties were critical to the creation of structures such as galaxies—within the (relatively short) time span we know to be a typical galaxy lifetime—and, in particular, to the formation of a galaxy the size of the Milky Way. Without dark matter, radiation would have prevented clumping of the galactic structure for too long, in essence wiping it out and keeping the universe smooth and homogeneous. The galaxy essential to our solar system and our life was formed in the time since the big bang only because of the existence of dark matter.

Some people, on first hearing about dark matter, feel dismayed. How can something we do not see exist? At least since the Copernican revolution, humans should be prepared to admit their noncentrality to the makeup of the universe. Yet each time people learn about it in a new context, many get confused or surprised. There is no reason that the matter we see should be the only type of matter there is. The existence of dark matter might be expected and is compatible with everything we know.

Perhaps some confusion lies in the name. Dark matter should really be called transparent matter because, as with all transparent things, light just passes through it. Nevertheless, its nature is far from transparent. Physicists and astronomers would like to understand, at a more fundamental level, what exactly dark matter is. Is it made up of a new type of fundamental particle, or does it consist of some invisible, compact object, such as a black hole? If it is a particle, does it have any (albeit very weak) interaction with familiar matter, aside from gravity? Does that particle have any interactions with itself that would be invisible to our senses? Is there more than one type of such a particle? Do any of these particles have interactions of any sort?

My theoretical colleagues and I have thought about a number of interesting possibilities. Ultimately, however, we will learn about the true nature of dark matter only with the help of further observations to guide us. Those observations might consist of more detailed measurements of dark matter's gravitational influence. Or—if we are very lucky and dark matter does have some tiny, nongravitational interaction with ordinary matter we have so far failed to observe—big underground detectors, satellites in space or the Large Hadron Collider at CERN near Geneva might in the future detect dark matter particles. Even without such interactions with ordinary matter, dark matter's self-interactions might have observable consequences. For example, the internal structure of galaxies at small scales will be different if dark matter's interactions with itself rearrange matter at galactic centers. Compact or other structures akin to the Milky Way, such as the bright gas clouds and stars we see when we look at the night sky, could indicate one or more distinct species of dark matter particles that interact with one another. Or hypothesized particles called axions that interact with magnetic fields might be detected in laboratories or in space.

For a theorist, an observer or an experimentalist, dark matter is a promising target for research. We know it exists, but we do not yet know what it is at a fundamental level. The reason we do not know might be obvious by now: it is just not interacting enough to tell us, at least so far. As humans, we can only do so much if ordinary matter is essentially oblivious to anything but dark matter's very existence. But if dark matter has some more interesting properties, researchers are poised to find them—and, in the process, to help us more completely address this wonderful mystery.

Lisa Randall is Frank B. Baird, Jr., Professor of Science at Harvard University. She serves on *Scientific American*'s board of advisers. Among her many books is *Dark Matter and the Dinosaurs: The Astounding Interconnectedness of the Universe* (2015).

NEUROSCIENCE

What Is Consciousness?

Scientists are beginning to unravel a mystery that has long vexed philosophers

By Christof Koch

CONSCIOUSNESS IS EVERYTHING YOU experience. It is the tune stuck in your head, the sweetness of chocolate mousse, the throbbing pain of a toothache, the fierce love for your child and the bitter knowledge that eventually all feelings will end.

The origin and nature of these experiences, sometimes referred to as qualia, have been a mystery from the earliest days of antiquity right up to the present. Many modern analytic philosophers of mind, most prominently perhaps Daniel Dennett of Tufts University, find the existence of consciousness such an intolerable affront to what they believe should be a meaningless universe of matter and the void that they declare it to be an illusion. That is, they either deny that qualia exist or argue that they can never be meaningfully studied by science.

If that assertion was true, this essay would be very short. All I would need to explain is why you, I and most everybody else is so convinced that we have feelings at all. If I have a tooth abscess, however, a sophisticated argument to persuade me that my pain is delusional will not lessen its torment one iota. As I have very little sympathy for this desperate solution to the mind-body problem, I shall move on.

The majority of scholars accept consciousness as a given and seek to understand its relationship to the objective world described by science. More than a quarter of a century ago Francis Crick and I decided to set aside philosophical discussions on consciousness (which have engaged scholars since at least the time of Aristotle) and instead search for its physical footprints. What is it about a highly excitable piece of brain matter that gives rise to consciousness? Once we can understand that, we hope to get closer to solving the more fundamental problem.

We seek, in particular, the neuronal correlates of consciousness (NCC), defined as the minimal neuronal mechanisms jointly sufficient for any specific conscious experience. What must happen in your brain for you to experience a toothache, for example? Must some nerve cells vibrate at some magical frequency? Do some special "consciousness neurons" have to be activated? In which brain regions would these cells be located?

NEURONAL CORRELATES OF CONSCIOUSNESS

WHEN DEFINING THE NCC, the qualifier "minimal" is important. The brain as a whole can be considered an NCC, after all: it generates experience, day in and day out. But the seat of consciousness can be further ring-fenced. Take the spinal cord, a foot-and-a-half-long flexible tube of nervous tissue inside the backbone with about a billion nerve cells. If the spinal cord is completely severed by trauma to the neck region, victims are paralyzed in legs, arms and torso, unable to control their bowel and bladder, and without bodily sensations. Yet these tetraplegics continue to experience life in all its variety—they see, hear, smell, feel emotions and remember as much as before the incident that radically changed their life.

Or consider the cerebellum, the "little brain" underneath the back of the brain. One of the most ancient brain circuits in evolutionary terms, it is involved in motor control, posture and gait and in the fluid execution of complex sequences of motor movements. Playing the piano, typing, ice dancing or climbing a rock wall—all these activities involve the cerebellum. It has the brain's most glorious neurons, called Purkinje cells, which possess tendrils that spread like a sea fan coral and harbor complex electrical dynamics. It also has by far the most neurons, about 69 billion (most of which are the star-shaped cerebellar granule cells), four times more than in the rest of the brain combined.

What happens to consciousness if parts of the cerebellum are lost to a stroke or to the surgeon's knife? Very little! Cerebellar patients complain of several deficits, such as the loss of fluidity of piano playing or keyboard typing but never of losing any aspect of their consciousness. They hear, see and feel fine, retain a sense of self, recall past events and continue to project themselves into the future. Even being born without a cerebellum does not appreciably affect the conscious experience of the individual.

All of the vast cerebellar apparatus is irrelevant to subjective experience. Why? Important hints can be found within its circuitry, which is exceedingly uniform and parallel (just as batteries may be connected in parallel). The cerebellum is almost exclusively a feed-forward circuit: one set of neurons feeds the next, which in turn influences a third set. There are no complex feedback loops that reverberate with electrical activity passing back and forth. (Given the time needed for a conscious perception to develop, most theoreticians infer that it must involve feedback loops within the brain's cavernous circuitry.) Moreover, the cerebellum is functionally divided into hundreds or more independent computational modules. Each one operates in parallel, with distinct, nonoverlapping inputs and output, controlling movements of different motor or cognitive systems. They scarcely interact—another feature held indispensable for consciousness.

One important lesson from the spinal cord and the cerebellum is that the genie of consciousness does not just appear when any neural tissue is excited. More is needed. This additional factor is found in the gray matter making up the celebrated cerebral cortex, the outer surface of the brain. It is a laminated sheet of intricately interconnected nervous tissue, the size and width of a 14-inch pizza. Two of these sheets, highly folded, along with their hundreds of millions of wires—the white matter—are crammed into the skull. All available evidence implicates neocortical tissue in generating feelings.

We can narrow down the seat of consciousness even further. Take, for example, experiments in which different stimuli are presented to the right and the left eyes. Suppose a picture of Donald Trump is visible only to your left eye and one of Hillary Clinton only to your right eye. We might imagine that you would see some weird superposition of Trump and Clinton. In reality, you will see Trump for a few seconds, after which he will disappear and Clinton will appear, after which she will go away and Trump will reappear. The two images will alternate in a never-ending dance because of what neuroscientists call binocular rivalry. Because your brain is getting an ambiguous input, it cannot decide: Is it Trump, or is it Clinton?

If, at the same time, you are lying inside a magnetic scanner that registers brain activity, experimenters will find that a broad set of cortical regions, collectively known as the posterior hot zone, is active. These are the parietal, occipital and temporal regions in the posterior part of cortex [*see box on opposite page*] that play the most significant role in tracking what we see. Curiously, the primary visual cortex that receives and passes on the information streaming up from the eyes does not signal what the subject sees. A similar hierarchy of labor appears to be true of sound and touch: primary auditory and primary somatosensory cortices do not directly contribute to the content of auditory or somatosensory experience. Instead it is the next stages of processing—in the posterior hot zone—that give rise to conscious perception, including the image of Trump or Clinton.

More illuminating are two clinical sources of causal evidence: electrical stimulation of cortical tissue and the study of patients following the loss of specific regions caused by injury or disease. Before removing a brain tumor or the locus of a patient's epileptic seizures, for example, neurosurgeons map the functions of nearby cortical tissue by directly stimulating it with electrodes. Stimulating the posterior hot zone can trigger a diversity of distinct sensations and feelings. These could be flashes of light, geometric shapes, distortions of faces, auditory or visual hallucinations, a feeling of familiarity or unreality, the urge to move a specific limb, and so on. Stimulating the front of the cortex is a different matter: by and large, it elicits no direct experience.

A second source of insights are neurological patients from the first half of the 20th century. Surgeons sometimes had to excise a large belt of prefrontal cortex to remove tumors or to ameliorate epileptic seizures. What is remarkable is how unremarkable these patients appeared. The loss of a portion of the frontal lobe did have certain deleterious effects: the patients developed a lack of inhibition of inappropriate emotions or actions, motor deficits, or uncontrollable repetition of specific action or words. Following the operation, however, their personality and IQ improved, and they went on to live for many more years, with no evidence that the drastic removal of frontal tissue significantly affected their conscious experience. Conversely, removal of even small regions of the posterior cortex, where the hot zone resides, can lead to a loss of entire classes of conscious content: patients are unable to recognize faces or to see motion, color or space.

So it appears that the sights, sounds and other sensations of life as we experience it are generated by regions within the posterior cortex. As far as we can tell, almost all conscious experiences have their origin there. What is the crucial difference between these posterior regions and much of the prefrontal cortex, which does not directly contribute to subjective content? The truth is that we do not know. Even so—and excitingly—a recent finding indicates that neuroscientists may be getting closer.

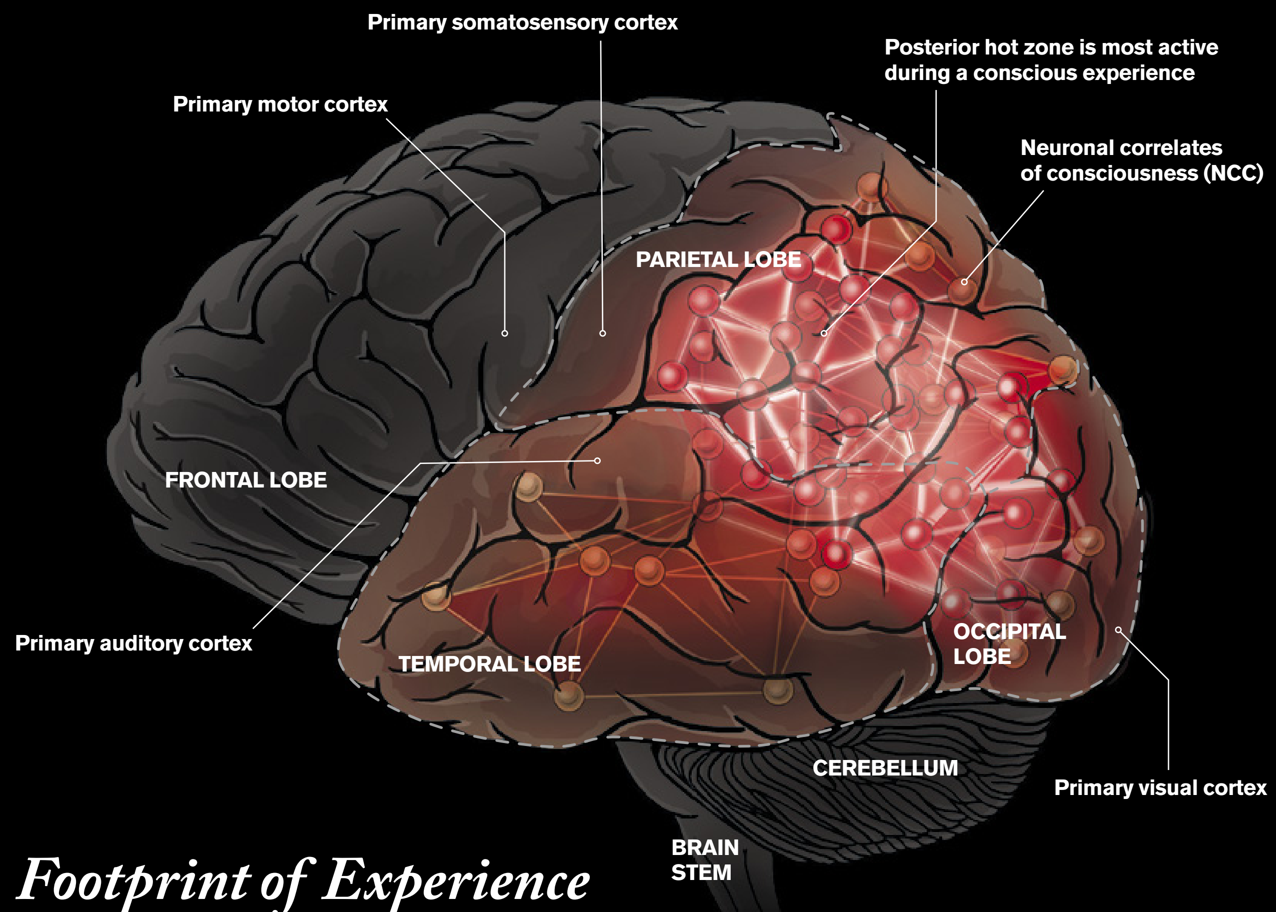
THE CONSCIOUSNESS METER

AN UNMET CLINICAL NEED exists for a device that reliably detects the presence or absence of consciousness in impaired or incapacitated individuals. During surgery, for example, patients are anesthetized to keep them immobile and their blood pressure stable and to eliminate pain and traumatic memories. Unfortunately, this goal is not always met: every year hundreds of patients have some awareness under anesthesia.

Another category of patients, who have severe brain injury because of accidents, infections or extreme intoxication, may live for years without being able to speak or respond to verbal requests. Establishing that they experience life is a grave challenge to the clinical arts. Think of an astronaut adrift in space, listening to mission control's attempts to contact him. His damaged radio does not relay his voice, and he appears lost to the world. This is the forlorn situation of patients whose damaged brain will not let them communicate to the world—an extreme form of solitary confinement.

In the early 2000s Giulio Tononi of the University of Wisconsin–Madison and Marcello Massimini, now at the University of Milan in Italy, pioneered a technique, called zap and zip, to probe whether someone is conscious or not. The scientists held a sheathed coil of wire against the scalp and "zapped" it—sent an intense pulse of magnetic energy into the skull—inducing a brief electric current in the neurons underneath. The perturbation, in turn, excited and inhibited the neurons' partner cells in connected regions, in a chain reverberating across the cortex, until the activity died out. A network of electroencephalogram (EEG) sensors, positioned outside the skull, recorded these electrical signals. As they unfolded over time, these traces, each corresponding to a specific location in the brain below the skull, yielded a movie.

These unfolding records neither sketched a stereotypical pattern, nor were they completely random. Remarkably, the more predictable these waxing and waning rhythms were, the more likely the brain was unconscious. The researchers quantified this intuition by



Footprint of Experience

Conscious awareness is closely associated with the cerebral cortex, an intricately folded and connected sheet of nervous tissue. Each experience corresponds to a specific set of neural activities, called the neuronal correlates of consciousness (NCC), in a posterior hot zone of the brain that consists of the parietal, occipital and temporal lobes of the cerebral cortex. Complexity of the neural excitations after a magnetic pulse yields a measure of the degree to which a person is conscious.

compressing the data in the movie with an algorithm commonly used to "zip" computer files. The zipping yielded an estimate of the complexity of the brain's response. Volunteers who were awake turned out have a "perturbational complexity index" of between 0.31 and 0.70, dropping to below 0.31 when deeply asleep or anesthetized. Massimini and Tononi tested this zap-and-zip measure on 48 patients who were brain-injured but responsive and awake, finding that in every case, the method confirmed the behavioral evidence for consciousness.

The team then applied zap and zip to 81 patients who were minimally conscious or in a vegetative state. For the former group, which showed some signs of nonreflexive behavior, the method correctly found 36 out of 38 patients to be conscious. It misdiagnosed two patients as unconscious. Of the 43 vegetative-state patients in which all bedside attempts to establish communication failed, 34 were labeled as unconscious, but nine were not. Their brains responded similarly to those of conscious controls—implying that they were conscious yet unable to communicate with their loved ones.

Ongoing studies seek to standardize and improve zap and zip for neurological patients and to extend it to psychiatric and pediatric patients. Sooner or later scientists will discover the specific set of neural mechanisms that give rise to any one experience. Although these findings will have important clinical implications and may give succor to families and friends, they will not answer some fundamental questions: Why these neurons and not those? Why this particular frequency and not that? Indeed, the abiding mystery is how and why any highly organized piece of active matter gives rise to conscious sensation. After all, the brain is like any other organ, subject to the same physical laws as the heart or the liver. What makes it different? What is it about the biophysics of a chunk of highly excitable brain matter that turns gray goo into the glorious surround sound and Technicolor that is the fabric of everyday experience?

Ultimately what we need is a satisfying scientific theory of consciousness that predicts under which conditions any particular physical system—whether it is a complex circuit of neurons or silicon transistors—has experiences. Furthermore, why does the quality of these experiences differ? Why does a clear blue sky feel so different from the screech of a badly tuned violin? Do these differences

Illustration by Mesa Schumacher

in sensation have a function, and if so, what is it? Such a theory will allow us to infer which systems will experience anything. Absent a theory with testable predictions, any speculation about machine consciousness is based solely on our intuition, which the history of science has shown is not a reliable guide.

What is it about the biophysics of a chunk of brain matter that turns gray goo into the glorious surround sound and Technicolor that is the fabric of everyday experience?

Fierce debates have arisen around the two most popular theories of consciousness. One is the global neuronal workspace (GNW) by psychologist Bernard J. Baars and neuroscientists Stanislas Dehaene and Jean-Pierre Changeux. The theory begins with the observation that when you are conscious of something, many different parts of your brain have access to that information. If, on the other hand, you act unconsciously, that information is localized to the specific sensory motor system involved. For example, when you type fast, you do so automatically. Asked how you do it, you would not know: you have little conscious access to that information, which also happens to be localized to the brain circuits linking your eyes to rapid finger movements.

TOWARD A FUNDAMENTAL THEORY

GNW ARGUES THAT CONSCIOUSNESS ARISES from a particular type of information processing—familiar from the early days of artificial intelligence, when specialized programs would access a small, shared repository of information. Whatever data were written onto this "blackboard" became available to a host of subsidiary processes: working memory, language, the planning module, and so on. According to GNW, consciousness emerges when incoming sensory information, inscribed onto such a blackboard, is broadcast globally to multiple cognitive systems—which process these data to speak, store or call up a memory or execute an action.

Because the blackboard has limited space, we can only be aware of a little information at any given instant. The network of neurons that broadcast these messages is hypothesized to be located in the frontal and parietal lobes. Once these sparse data are broadcast on this network and are globally available, the information becomes conscious. That is, the subject becomes aware of it. Whereas current machines do not yet rise to this level of cognitive sophistication, this is only a question of time. GNW posits that computers of the future will be conscious.

Integrated information theory (IIT), developed by Tononi and his collaborators, including me, has a very different starting point: experience itself. Each experience has certain essential properties. It is intrinsic, existing only for the subject as its "owner"; it is structured (a yellow cab braking while a brown dog crosses the street); and it is specific—distinct from any other conscious experience, such as a particular frame in a movie. Furthermore, it is unified and definite. When you sit on a park bench on a warm, sunny day, watching children play, the different parts of the experience—the breeze playing in your hair or the joy of hearing your toddler laugh—cannot be separated into parts without the experience ceasing to be what it is.

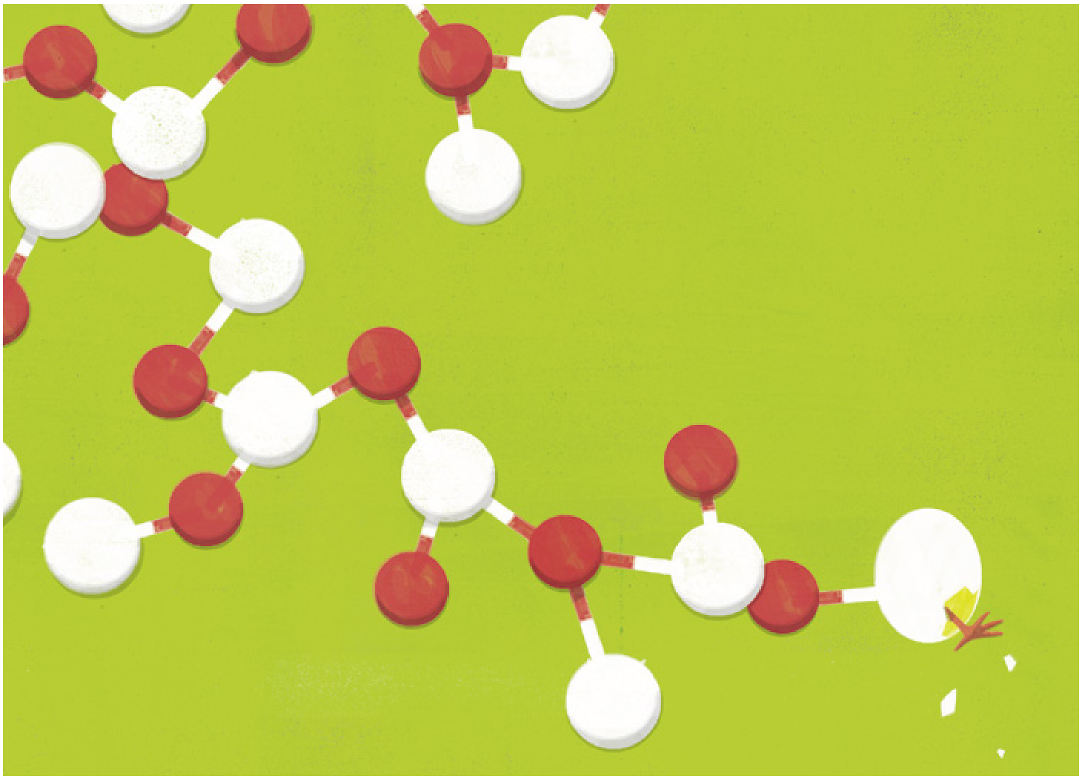
Tononi postulates that any complex and interconnected mechanism whose structure encodes a set of cause-and-effect relationships will have these properties—and so will have some level of consciousness. It will feel like something from the inside. But if, like the cerebellum, the mechanism lacks integration and complexity, it will not be aware of anything. As IIT states it, consciousness is intrinsic causal power associated with complex mechanisms such as the human brain.

IIT theory also derives, from the complexity of the underlying interconnected structure, a single nonnegative number Φ (pronounced "*fy*") that quantifies this consciousness. If Φ is zero, the system does not feel like anything to be itself. Conversely, the bigger this number, the more intrinsic causal power the system possesses and the more conscious it is. The brain, which has enormous and highly specific connectivity, possesses very high Φ, which implies a high level of consciousness. IIT explains a number of observations, such as why the cerebellum does not contribute to consciousness and why the zap-and-zip meter works. (The quantity the meter measures is a very crude approximation of Φ.)

IIT also predicts that a sophisticated simulation of a human brain running on a digital computer cannot be conscious—even if it can speak in a manner indistinguishable from a human being. Just as simulating the massive gravitational attraction of a black hole does not actually deform spacetime around the computer implementing the astrophysical code, programming for consciousness will never create a conscious computer. Consciousness cannot be computed: it must be built into the structure of the system.

Two challenges lie ahead. One is to use the increasingly refined tools at our disposal to observe and probe the vast coalitions of highly heterogeneous neurons making up the brain to further delineate the neuronal footprints of consciousness. This effort will take decades, given the byzantine complexity of the central nervous system. The other is to verify or falsify the two, currently dominant, theories. Or, perhaps, to construct a better theory out of fragments of these two that will satisfactorily explain the central puzzle of our existence: how a three-pound organ with the consistency of tofu exudes the feeling of life.

Christof Koch is chief scientist and president of the Allen Institute for Brain Science in Seattle. He serves on *Scientific American*'s board of advisers and has authored many books, including *Consciousness: Confessions of a Romantic Reductionist* (2012).



How Did Life Begin?

Untangling the origins of organisms will require experiments at the tiniest scales and observations at the vastest

By Jack Szostak

Is the existence of life on Earth a lucky fluke or an inevitable consequence of the laws of nature? Is it simple for life to emerge on a newly formed planet, or is it the virtually impossible product of a long series of unlikely events? Advances in fields as disparate as astronomy, planetary science and chemistry now hold promise that answers to such profound questions may be around the corner. If life turns out to have emerged multiple times in our galaxy, as scientists are hoping to discover, the path to it cannot be so hard. Moreover, if the route from chemistry to biology proves simple to traverse, the universe could be teeming with life.

The discovery of thousands of exoplanets has sparked a renaissance in origin-of-life studies. In a stunning surprise, almost all the newly discovered solar systems look very different from our own. Does that mean something about our own, very odd, system favors the emergence of life? Detecting signs of life on a planet orbiting a distant star is not going to be easy, but the technology for teasing out subtle "biosignatures" is developing so rapidly that with luck we may see distant life within one or two decades.

To understand how life might begin, we first have to figure out how—and with what ingredients—planets form. A new generation of radio telescopes, notably the Atacama Large Millimeter/submillimeter Array in Chile's Atacama Desert, has provided beautiful images of protoplanetary disks and maps of their chemical composition. This information is inspiring better models of how planets assemble from the dust and gases of a disk. Within our own solar system, the Rosetta mission has visited a comet, and OSIRIS-REx will visit, and even try to return samples from, an asteroid, which might give us the essential inventory of the materials that came together in our planet.

Once a planet like our Earth—not too hot and not too cold, not too dry and not too wet—has formed, what chemistry must develop to yield the building blocks of life? In the 1950s the iconic Miller-Urey experiment, which zapped a mixture of water and simple chemicals with electric pulses (to simulate the impact of lightning), demonstrated that amino acids, the building blocks of proteins, are easy to make. Other molecules of life turned out to be harder to synthesize, however, and it is now apparent that we need to completely reimagine the path from chemistry to life. The central reason hinges on the versatility of RNA, a very long molecule that plays a multitude of essential roles in all existing forms of life. RNA can not only act like an enzyme, it can also store and transmit information. Remarkably, all the protein in all organisms is made by the catalytic activity of the RNA component of the ribosome, the cellular machine that reads genetic information and makes protein molecules. This observation suggests that RNA dominated an early stage in the evolution of life.

Today the question of how chemistry on the infant Earth gave rise to RNA and to RNA-based cells is the central question of origin-of-life research. Some scientists think that life originally used simpler molecules and only later evolved RNA. Other researchers, however, are tackling the origin of RNA head-on, and exciting new ideas are revolutionizing this once quiet backwater of chemical research. Favored geochemical scenarios involve volcanic regions or impact craters, with complex organic chemistry, multiple sources of energy, and dynamic light-dark, hot-cold and wet-dry cycles. Strikingly, many of the chemical intermediates on the way to RNA crystallize out of reaction mixtures, self-purifying and potentially accumulating on the early Earth as organic minerals—reservoirs of material waiting to come to life when conditions change.

Assuming that key problem is solved, we will still need to understand how RNA was replicated within the first primitive cells. Researchers are just beginning to identify the sources of chemical energy that could enable the RNA to copy itself, but much remains to be done. If these hurdles can also be overcome, we may be able to build replicating, evolving RNA-based cells in the laboratory—recapitulating a possible route to the origin of life.

What next? Chemists are already asking whether our kind of life can be generated only through a single plausible pathway or whether multiple routes might lead from simple chemistry to RNA-based life and on to modern biology. Others are exploring variations on the chemistry of life, seeking clues as to the possible diversity of life "out there" in the universe. If all goes well, we will eventually learn how robust the transition from chemistry to biology is and therefore whether the universe is full of life-forms or—but for us—sterile.

Jack Szostak is a professor of genetics at Harvard Medical School and one of the recipients of the 2009 Nobel Prize in Physiology or Medicine.

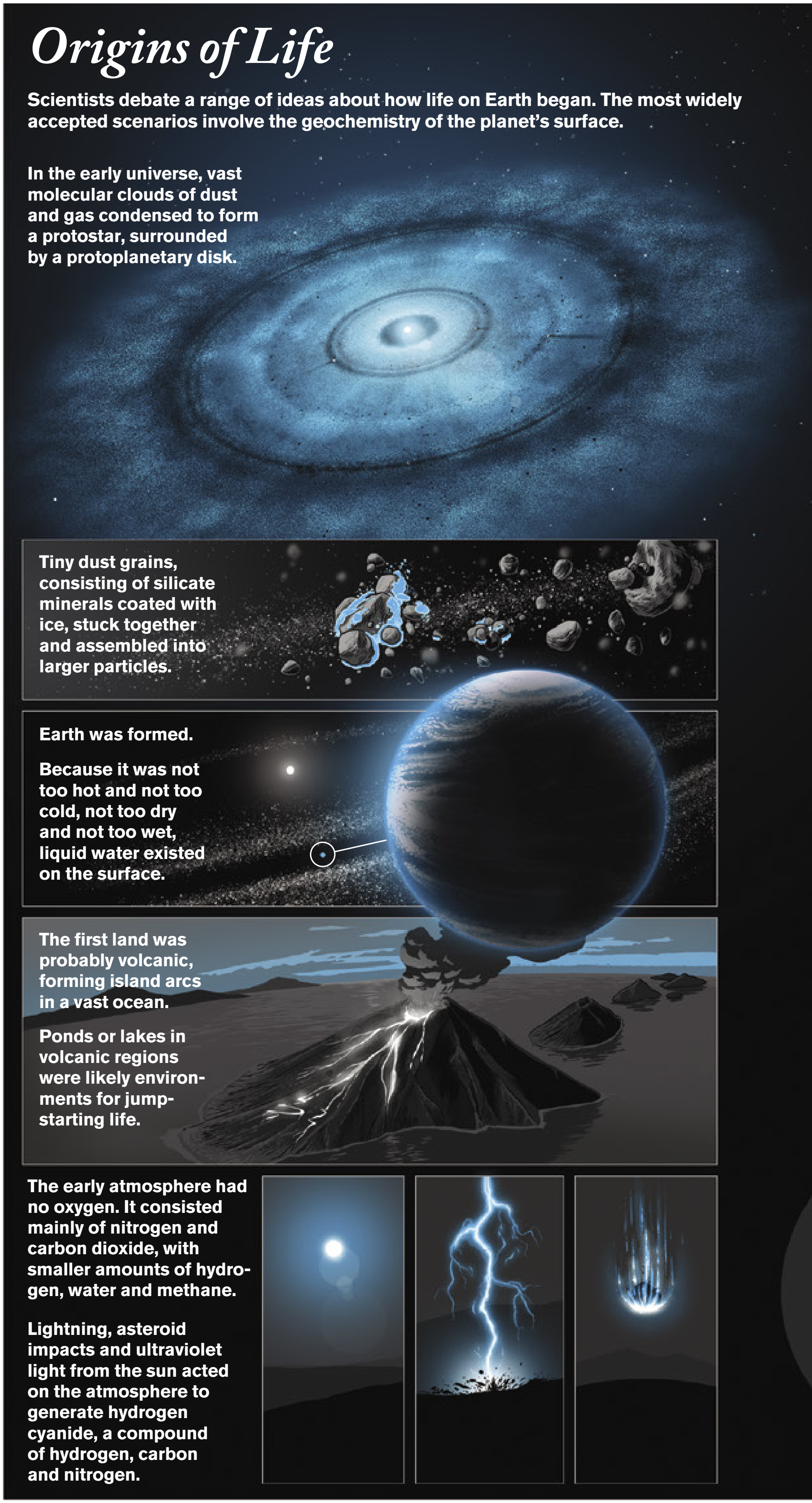
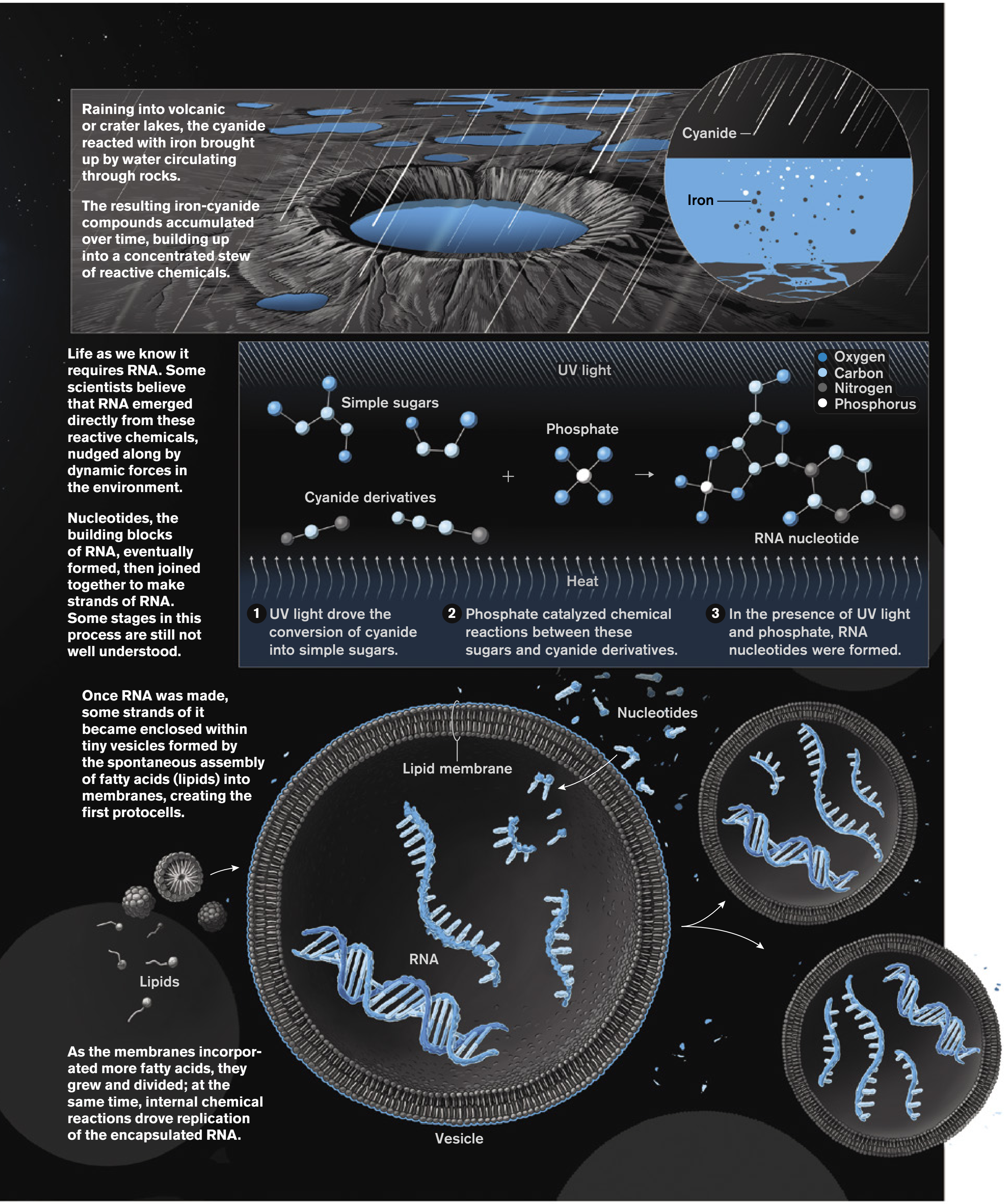
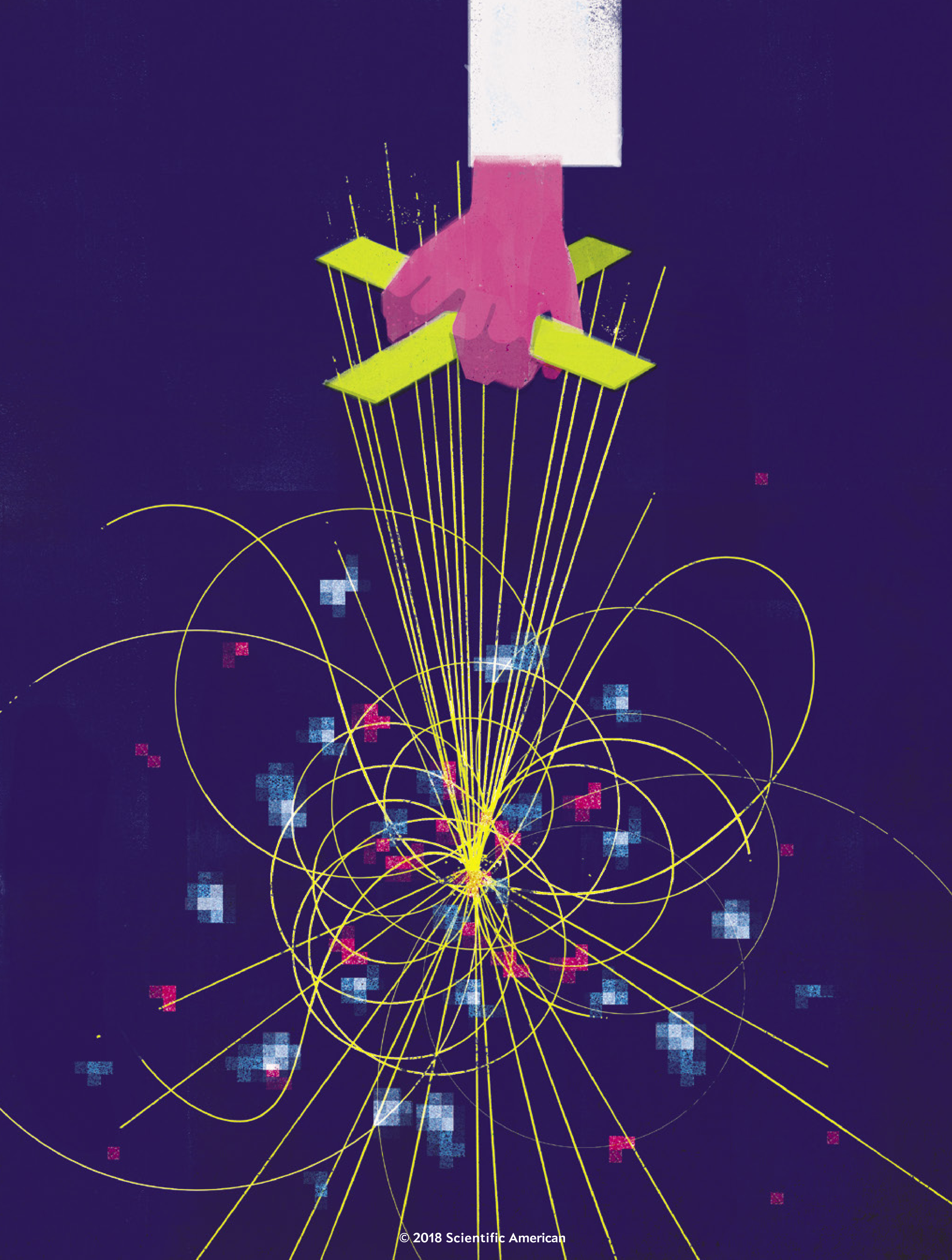


Illustration by Matthew Twombly


Raining into volcanic or crater lakes, the cyanide reacted with iron brought up by water circulating through rocks.
The resulting iron-cyanide compounds accumulated over time, building up into a concentrated stew of reactive chemicals.
Cyanide
Iron
Life as we know it requires RNA. Some scientists believe that RNA emerged directly from these reactive chemicals, nudged along by dynamic forces in the environment.
Nucleotides, the building blocks of RNA, eventually formed, then joined together to make strands of RNA. Some stages in this process are still not well understood.
UV light
Oxygen
Carbon
Nitrogen
Phosphorus
Simple sugars
Phosphate
Cyanide derivatives
RNA nucleotide
Heat
1 UV light drove the conversion of cyanide into simple sugars.
2 Phosphate catalyzed chemical reactions between these sugars and cyanide derivatives.
3 In the presence of UV light and phosphate, RNA nucleotides were formed.
Once RNA was made, some strands of it became enclosed within tiny vesicles formed by the spontaneous assembly of fatty acids (lipids) into membranes, creating the first protocells.
Nucleotides
Lipid membrane
RNA
Lipids
Vesicle
As the membranes incorporated more fatty acids, they grew and divided; at the same time, internal chemical reactions drove replication of the encapsulated RNA.



NANOSCIENCE

What Are the Limits of Manipulating Nature?

By reaching down into the quantum world, scientists are hoping to gain more control over matter and energy

By Neil Savage

MATT TRUSHEIM FLIPS A SWITCH in the darkened laboratory, and an intense green laser illuminates a tiny diamond locked in place beneath a microscope objective. On a computer screen an image appears, a fuzzy green cloud studded with brighter green dots. The glowing dots are color centers in the diamond—tiny defects where two carbon atoms have been replaced by a single atom of tin, shifting the light passing through from one shade of green to another.

Later, that diamond will be chilled to the temperature of liquid helium. By controlling the crystal structure of the diamond on an atom-by-atom level, bringing it to within a few degrees of absolute zero and applying a magnetic field, researchers at the Quantum Photonics Laboratory run by physicist Dirk Englund at the Massachusetts Institute of Technology think they can select the quantum-mechanical properties of photons and electrons with such precision that they can transmit unbreakable secret codes.

Trusheim, a postdoctoral researcher in the lab, is one of many scientists trying to figure out just which atoms embedded in which crystals under what conditions will give them that kind of control. Indeed, scientists around the world are tackling the hard problem of controlling nature at the level of atoms and below, down to electrons or even fractions of electrons. Their aim is to find the knobs that control the fundamental properties of matter and energy and turn those knobs to customize matter and energy, creating ultrapowerful quantum computers or superconductors that work at room temperature.

These scientists face two main challenges. On a technical level, the work is extremely difficult. Some crystals, for instance, must be made to 99.99999999 percent purity in vacuum chambers emptier than space. The more fundamental challenge is that the quantum effects these researchers want to harness—for example, the ability of a particle to be in two states at once, à la Schrödinger's cat—happen at the level of individual electrons. Up here in the macro world, the magic goes away. Researchers manipulating matter at the smallest scales, therefore, are trying to coax nature into behaving in ways that strain at the limits imposed by fundamental physics. The degree to which they succeed will help determine our scientific understanding and technological capacity in the decades to come.

AN ALCHEMIST'S DREAM

MANIPULATING MATTER IS, to a significant degree, all about controlling electrons. After all, the behavior of the electrons in a material determines its properties as a whole—whether the substance is a metal, an insulator, a magnet, or something else. Some scientists are attempting to alter the collective behavior of electrons to create what is known as quantum synthetic materials. Researchers envision that "we can take an insulator and make it into a metal or a semiconductor and make it into a superconductor. We can turn a nonmagnetic material into a magnetic material," asserted physicist Eva Andrei of Rutgers University at a recent conference. "This is really an alchemist's dream come true."

The dream could lead to actual breakthroughs. For example, researchers have been trying for decades to create room-temperature superconductors, materials that could yield innovations such as electrical transmission lines that do not lose any energy. In a breakthrough in 1957 that earned them a Nobel Prize in 1972, physicists John Bardeen, Leon Cooper and John Robert Schrieffer demonstrated that superconductivity arises when the free electrons in a metal such as aluminum align into so-called Cooper pairs. Even if they are relatively far apart, each electron is matched with another that has the opposite spin and momentum. Rather like couples dancing in a crowded disco, the paired electrons' motions are coordinated with each other even if other electrons come between them.

This arrangement allows current to flow through a material with no resistance and therefore no loss. The only practical superconductors developed thus far must be cooled to within a few degrees of absolute zero before this state takes hold. Yet recently researchers have found that hitting a material with a high-intensity laser can also knock electrons into Cooper pairs, if only briefly. David Hsieh, a condensed matter physicist at the California Institute of Technology, creates photoinduced superconductivity in a type of material (known as a Mott insulator) that becomes insulating at very cold temperatures. Light striking the insulator excites the electrons, causing them to briefly align. "The shaking needs to be done very violently," Hsieh explains. "Momentarily, the electric field is extremely strong—but it's only on for such a short time [that] it's not delivering that much heat."

To keep the laser from vaporizing the material, Hsieh strikes it with a pulse that lasts only tens or hundreds of femtoseconds. (There are as many femtoseconds in one second as there are seconds in 32 million years.) Unfortunately, the superconductivity thereby induced does not last much longer. The challenge for researchers pursuing similar work is to figure out how to make the effect last long enough to be useful. Hsieh says of this and other studies of quantum materials: "What we're trying to do is dream up host compounds in which even when you're talking about a large batch of electrons, that quantum-mechanical weirdness that typically is confined to single particles is still retained."

UNBREAKABLE CODES

CONTROLLING ELECTRONS is also how Trusheim and Englund hope to develop unbreakable quantum encryption. In their case, the goal is not to change the properties of materials but to share the quantum properties of electrons within their engineered diamonds with photons that transmit the cryptographic key. Rattling around in the color centers of the diamonds in Englund's lab are free electrons, the spins of which can be measured by probing them with a strong magnetic field. A spin that is aligned with the field can be called spin 1, and a spin that is not aligned is spin 2—equivalent to the 1 and 0 of a digital bit. "It's a quantum particle, so it can be in both states at the same time," Englund says. That makes it a quantum bit, or qubit, capable of making multiple calculations simultaneously.

This is where a mysterious property known as quantum entanglement comes in. Imagine a box containing a red ball and a blue ball. You can reach in without looking, take one ball and put it in your pocket, then travel across town. You then take the ball out of your pocket and discover that it is red. That immediately tells you that the ball back in the box is blue. That is entanglement. This effect, translated to a quantum realm, can transmit information instantaneously and across vast distances.

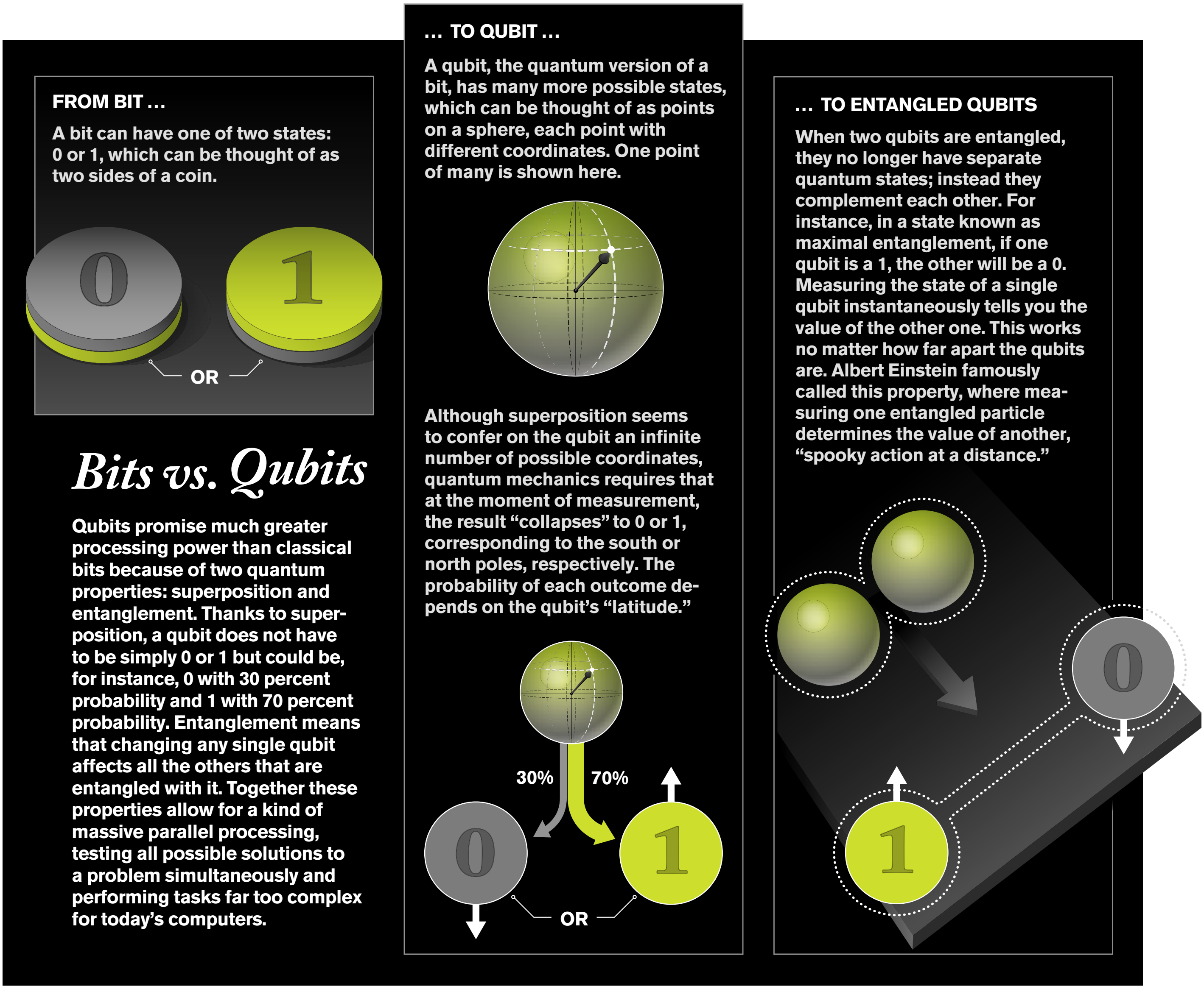
The color centers in the diamonds in Englund's lab transfer the quantum states of the electrons contained within to photons by means of entanglement, creating what Englund calls "flying qubits." As in standard optical communications, a photon can be transmitted to a receiver—in this case, another diamond vacancy—and its quantum state transferred to a new electron, so the two electrons become correlated. The transmission of such entangled bits allows two people to share a cryptographic key. "Each one has a string of 0s and 1s, or ups and downs of the spin, that look locally random, but they're identical," Englund says. Using that key as a multiplication factor for other data they send lets them communicate securely. If an eavesdropper were to intercept the transmission, the senders would know because the act of measuring a quantum state changes it.

Englund is experimenting with a quantum network that sends photons over optical fibers between his lab, a facility down the road at Harvard University, and another at M.I.T.'s Lincoln Laboratory in the nearby town of Lexington, Mass. Researchers have already succeeded in transmitting quantum-cryptographic keys over greater distances—in 2017 Chinese scientists reported having transmitted such a key from a satellite in Earth orbit to two ground stations 1,200 kilometers apart in the mountains of Tibet. But the bit rate of the Chinese experiment was too low for practical communications: the researchers detected only one entangled pair out of six million. The innovation that will make ground-based quantum-cryptographic networks practical are quantum repeaters—devices placed at intervals throughout the network that boost the signal without interfering with its quantum properties. Englund's goal is to find materials with just the right atomic defects to form the heart of those quantum repeaters.

The trick is making enough spin-entangled photons to carry the data. The electron in a nitrogen vacancy maintains its spin state for a long time—about a second—increasing the number of chances for laser light passing through to produce an entangled photon. But nitrogen is a small atom, and it does not fill the space created by the missing carbons. This misfit can cause subsequent photons to be of slightly different colors, so they no longer match one another. Other atoms, such as tin, nestle snugly and produce a stable wavelength. But those atoms do not hold their spin as long—hence the work continues to find the perfect balance.

SPLIT ENDS

WHILE ENGLUND AND OTHERS wrestle with individual electrons, some scientists are diving even deeper into the quantum world and trying to manipulate mere fractions of electrons. This work has its roots in an experiment conducted in 1982, when scientists from Bell Laboratories and Lawrence Livermore National Laboratory sandwiched two layers of different semiconductor crystals together, cooled them to near absolute zero and applied a strong magnetic field, trapping electrons in a plane at the interface between the two crystal layers. This arrangement created a kind of quantum soup, in which the movement of any given electron is influenced by the charges it feels from other electrons. "They're not really individual particles per se," says Michael Manfra, who runs the Quantum Semiconductor



Systems Group at Purdue University. "You can imagine a ballet where each dancer is not just doing their own thing, but they're responding to the motion of either their partner or the other dancers. There's this sort of generalized response."

The odd thing about this collection is that it can have fractional charges. An electron is an indivisible unit—you cannot slice one into thirds—but a group of electrons in the right state can produce a so-called quasiparticle with a ⅓ charge. "It's as if electrons are fractionalized," says Mohammad Hafezi, a physicist at the Joint Quantum Institute, a research partnership between the University of Maryland and the National Institute of Standards and Technology. "It is very strange." Hafezi creates the effect in supercooled graphene, one-atom thick sheets of carbon, and he recently showed he could manipulate the movement of the quasiparticles by shining a laser on the graphene. "Now it's controllable," he says. "Now the external knobs I have, like the magnetic field and the light, can be tuned up and down. So the nature of that collective state changes."

Manipulating quasiparticles could allow for the creation of a special kind of qubit—a topological qubit. Topology is a field of mathematics that studies properties of an object that do not change even when that object is twisted or deformed. The standard example is a doughnut: if it were perfectly elastic, you could reshape it into a coffee cup without changing anything essential; the doughnut hole would take on a new role as the opening in the cup's handle. To change the doughnut to a pretzel, however, you would have to poke new holes into it, changing its topology.

A topological qubit retains its properties even under changing conditions. Normally particles change their quantum states, or "decohere," when disturbed by something in their environment, such as a tiny vibration caused by heat. But if you make a qubit

Illustration by Jen Christiansen

from two quasiparticles separated by some distance—say at opposite ends of a nanowire—you are essentially splitting an electron. Both "halves" would have to experience the exact same disturbance to decohere, and that is unlikely to happen by chance.

That property makes topological qubits attractive for quantum computers. Because of the ability of a qubit to be in a superposition of many states at once, quantum computers should be able to perform otherwise impossibly calculation-intensive tasks such as modeling the physics of the big bang. Manfra, in fact, is part of Microsoft's global effort to build quantum computers based on topological qubits. There are other, arguably easier approaches. Google and IBM, for example, are pursuing quantum computers based on wires supercooled to become semiconductors or ionized atoms in a vacuum chamber trapped by lasers. The problem with those approaches is that they are more sensitive to environmental perturbations than topological qubits, especially as the number of qubits grows.

Topological qubits could therefore herald a revolution in our ability to manipulate tiny things. There is, however, one significant problem: they do not yet exist. Researchers are struggling to construct them out of an object called a Majorana particle. Hypothesized by Ettore Majorana in 1937, this particle is its own antiparticle. An electron and its antiparticle, a positron, have identical properties except for charge, but the charge of the Majorana particle would be zero.

Scientists believe that certain configurations of electrons and holes (absences of electrons) can behave like Majorana particles. These, in turn, may one day be used as topological qubits. In 2012 physicist Leo Kouwenhoven of Delft University of Technology in the Netherlands and his colleagues measured what seemed to be Majorana particles in a network of superconducting and semiconducting nanowires. Still, argues Sankar Das Sarma of the Condensed Matter Theory Center at the University of Maryland, College Park, the only way to actually prove that these quasiparticles exist would be to build a topological qubit out of them.

Other experts in the field are optimistic, however. "I think without any question, eventually somebody will make a topological qubit, just because it's interesting to do, and they'll figure out how to do it," says Steve Simon, a condensed matter theorist at the University of Oxford. "The big question is, Is this the way we're going to build a quantum computer in the future?"

Quantum computers—along with high-temperature superconductors and unbreakable quantum encryption—may be years away, or they may never be achieved. But in the meantime, researchers will continue to struggle toward mastery of nature at the smallest scales. Scientists do not yet know how low they can go. They have gone surprisingly far, but the further down they get, the more nature pushes back.

Neil Savage is a science journalist in Lowell, Mass.

How Much Can We Know?

The reach of the scientific method is constrained by the limitations of our tools and the intrinsic impenetrability of some of nature's deepest questions

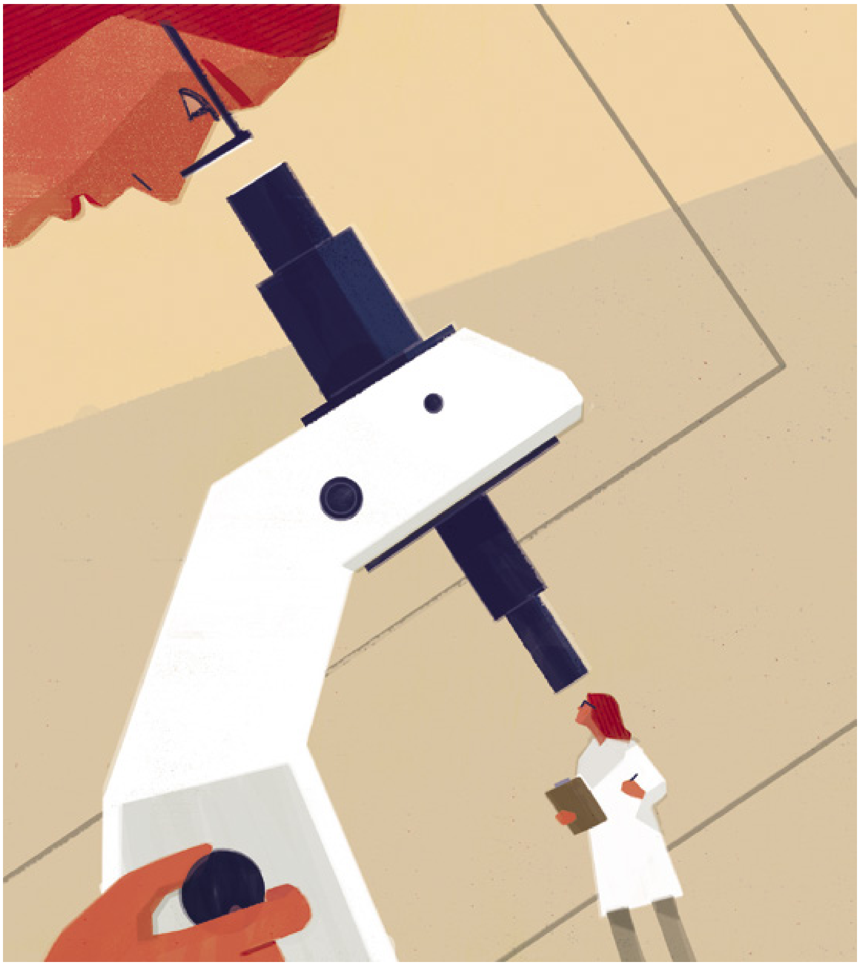
By Marcelo Gleiser

"What we observe is not nature in itself but nature exposed to our method of questioning," wrote German physicist Werner Heisenberg, who was the first to fathom the uncertainty inherent in quantum physics. To those who think of science as a direct path to the truth about the world, this quote must be surprising, perhaps even upsetting. Is Heisenberg saying that our scientific theories are contingent on us as observers? If he is, and we take him seriously, does this mean that what we call scientific truth is nothing but a big illusion?

People will quickly counterstrike with something like: Why do airplanes fly or antibiotics work? Why are we able to build machines that process information with such amazing efficiency? Surely, such inventions and so many others are based on laws of nature that function independently of us. There is order in the universe, and science gradually uncovers this order.

No question about it: There is order in the universe, and much of science is about finding patterns of behavior—from quarks to mammals to galaxies—that we translate into general laws. We strip away unnecessary complications and focus on what is essential, the core properties of the system we are studying. We then build a descriptive narrative of how the system behaves, which, in the best cases, is also predictive.

Often overlooked in the excitement of research is that the methodology of science requires interaction with the system we are studying. We observe its behavior, measure its properties, and build mathematical or conceptual models to understand it better. And to do this, we need tools that extend into



realms beyond our sensorial reach: the very small, the very fast, the very distant and the virtually inaccessible, such as what is inside the brain or buried in the earth's core. What we observe is not nature itself but nature as discerned through data we collect from machines. In consequence, the scientific worldview depends on the information we can acquire through our instruments. And given that our tools are limited, our view of the world is necessarily myopic. We can see only so far into the nature of things, and our ever shifting scientific worldview reflects this fundamental limitation on how we perceive reality.

Just think of biology before and after the microscope or gene sequencing, or of astronomy before and after the telescope, or of particle physics before and after colliders or fast electronics. Now, as in the 17th century, the theories we build and the worldviews we construct change as our tools of exploration transform. This trend is the trademark of science.

Sometimes people take this statement about the limitation of scientific knowledge as being defeatist: "If we can't get to the bottom of things, why bother?" This kind of response is misplaced. There is nothing defeatist in understanding the limitations of the scientific approach to knowledge. Science remains our best methodology to build consensus about the workings of nature. What should change is a sense of scientific triumphalism—the belief that no question is beyond the reach of scientific discourse.

There are clear unknowables in science—reasonable questions that, unless currently accepted laws of nature are violated, we cannot find answers to. One example is the multiverse: the conjecture that our universe is but one among a multitude of others, each potentially with a different set of laws of nature. Other universes lie outside our causal horizon, meaning that we cannot receive or send signals to them. Any evidence for their existence would be circumstantial: for example, scars in the radiation permeating space because of a past collision with a neighboring universe.

Other examples of unknowables can be conflated into three questions about origins: of the universe, of life and of the mind. Scientific accounts of the origin of the universe are incomplete because they must rely on a conceptual framework to even begin to work: energy conservation, relativity, quantum physics, for instance. Why does the universe operate under these laws and not others?

Similarly, unless we can prove that only one or very few biochemical pathways exist from nonlife to life, we cannot know for sure how life originated on Earth. For consciousness, the problem is the jump from the material to the subjective—for example, from firing neurons to the experience of pain or the color red. Perhaps some kind of rudimentary consciousness could emerge in a sufficiently complex machine. But how could we tell? How do we establish—as opposed to conjecture—that something is conscious?

Paradoxically, it is through our consciousness that we make sense of the world, even if only imperfectly. Can we fully understand something of which we are a part? Like the mythic snake that bites its own tail, we are stuck within a circle that begins and ends with our lived experience of the world. We cannot detach our descriptions of reality from how we experience reality. This is the playing field where the game of science unfolds, and if we play by the rules we can see only so much of what lies beyond.

Marcelo Gleiser is Appleton Professor of Natural Philosophy and a professor of physics and astronomy at Dartmouth College, where he directs the Institute for Cross-Disciplinary Engagement. He has authored several books, including *The Island of Knowledge: The Limits of Science and the Search for Meaning* (2014).

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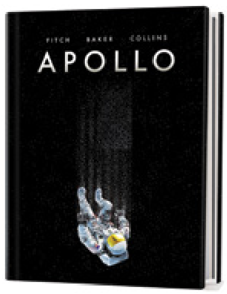
Apollo

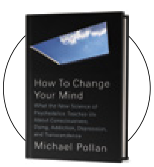
by Matt Fitch, Chris Baker and Mike Collins. SelfMadeHero, 2018 ($24.99)



The world waited anxiously during late July of 1969 for news of the first footsteps on the moon. Wives of the astronauts paced, President Richard Nixon in the White House mused on how the success or failure of the mission would play politically, and soldiers in the jungles of Vietnam compared themselves to the heroes in space. Writers Fitch and Baker teamed up with illustrator Collins (no relation to the Michael Collins, who flew with Neil Armstrong and Buzz Aldrin on the mission) to create a graphic novel of the suspense-filled story. They convey surprising depth and emotion, as well as rich historical details of the era. The book explores the political tension around the space program at the time, the nerve-wracking anxiety experienced by the families of the crew, and the heart-stopping moments of the mission that proved to be such a milestone.

How to Change Your Mind: What the New Science of Psychedelics Teaches Us about Consciousness, Dying, Addiction, Depression, and Transcendence

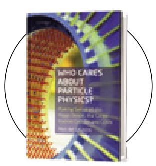
by Michael Pollan. Penguin Press, 2018 ($28)



A Swiss chemist took the first documented acid trip in April 1943. The researcher, Albert Hofmann, was synthesizing molecules from ergot—a fungus that commonly infects grains used for bread. He accidentally absorbed one of these compounds—lysergic acid diethylamide, LSD-25 for short—perhaps through his skin while working with it. Since then, psychedelic drugs have had a reputation mostly as a dangerous hippie pastime. Science writer Pollan examines what these chemicals might teach us about consciousness and the brain and even gives them a try himself—taking LSD in a yurt in an unnamed American mountain range under the guidance of a Bavarian ex-con.

Who Cares about Particle Physics? Making Sense of the Higgs Boson, the Large Hadron Collider and CERN

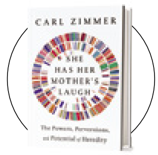
by Pauline Gagnon. Oxford University Press, 2018 (paperbound, $19.95)



Many people have heard the term "Higgs boson" and perhaps recall the hubbub when this particle was discovered in 2012. But how many really know what it is? Anyone wishing to bone up on particle physics would benefit from physicist Gagnon's book, which profiles the tiniest stuff in the universe. In addition to offering one of the most thorough yet accessible explanations of the Higgs boson, Gagnon—a former member of the ATLAS experiment at the Large Hadron Collider—gives an insider's account of the powerful accelerator where atoms crash together to create exotic particles. If theorists' hunches are borne out in ongoing experiments, she writes, "We are most likely on the verge of a huge scientific revolution." *—Clara Moskowitz*

She Has Her Mother's Laugh: The Powers, Perversions, and Potential of Heredity

by Carl Zimmer. Dutton, 2018 ($30)



Until the 19th-century revelation of heredity from Austrian monk Gregor Mendel, humankind mostly toyed with "genetics" through trial and error and guesswork. Since Mendel, scientists have figured out not only that sequences of DNA called genes encode traits such as eye color and height but that slight mistakes in those sequences can cause debilitating maladies. Science writer Zimmer threads together many intriguing narratives—each a story about how researchers tackled, and often misunderstood, heredity. From the horrors of eugenics to the discovery of a bacterial tool (the CRISPR/Cas9 complex) that snips away problematic DNA, he shows how our advancing knowledge of genetics continues to shape society and our very beings. *—Yasemin Saplakoglu*

Michael Shermer is publisher of *Skeptic* magazine (www.skeptic.com) and a Presidential Fellow at Chapman University. His new book is *Heavens on Earth: The Scientific Search for the Afterlife, Immortality, and Utopia.* Follow him on Twitter @michaelshermer

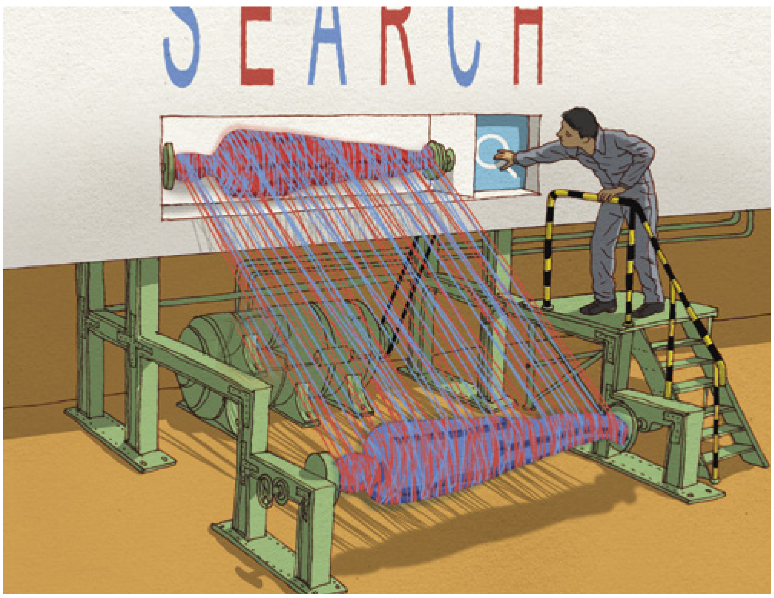
Soul-Searching

Google as a window into our private thoughts

By Michael Shermer

What are the weirdest questions you've ever Googled? Mine might be (for my latest book): "How many people have ever lived?" "What do people think about just before death?" and "How many bits would it take to resurrect in a virtual reality everyone who ever lived?" (It's 10 to the power of 10^{123}.) Using Google's autocomplete and Keyword Planner tools, U.K.-based Internet company Digitaloft generated a list of what it considers 20 of the craziest searches, including "Am I pregnant?" "Are aliens real?" "Why do men have nipples?" "Is the world flat?" and "Can a man get pregnant?"

This is all very entertaining, but according to economist Seth Stephens-Davidowitz, who worked at Google as a data scientist (he is now an op-ed writer for the *New York Times*), such searches may act as a "digital truth serum" for deeper and darker thoughts. As he explains in his book *Everybody Lies* (Dey Street Books, 2017), "In the pre-digital age, people hid their embarrassing thoughts from other people. In the digital age, they still hide them from other people, but not from the internet and in particular sites such as Google and PornHub, which protect their anonymity." Employing big data research tools "allows us to finally see what people really want and really do, not what they say they want and say they do."



People may tell pollsters that they are not racist, for example, and polling data do indicate that bigoted attitudes have been in steady decline for decades on such issues as interracial marriage, women's rights and gay marriage, indicating that conservatives today are more socially liberal than liberals were in the 1950s.

Using the Google Trends tool in analyzing the 2008 U.S. presidential election, however, Stephens-Davidowitz concluded that Barack Obama received fewer votes than expected in Democrat strongholds because of still latent racism. For example, he found that 20 percent of searches that included the N-word (hereafter, "n***") also included the word "jokes" and that on Obama's first election night about one in 100 Google searches with "Obama" in them included "kkk" or "n***(s)."

"In some states, there were more searches for '[n***] president' than 'first black president,'" he reports—and the highest number of such searches were not predominantly from Southern Republican bastions as one might predict but included upstate New York, western Pennsylvania, eastern Ohio, industrial Michigan and rural Illinois. This difference between public polls and private thoughts, Stephens-Davidowitz observes, helps to explain Obama's underperformance in regions with a lot of racist searches and partially illuminates the surprise election of Donald Trump.

But before we conclude that the arc of the moral universe is slouching toward Gomorrah, a Google Trends search for "n*** jokes," "bitch jokes" and "fag jokes" between 2004 and 2017, conducted by Harvard University psychologist Steven Pinker and reported in his 2018 book *Enlightenment Now,* shows downward-plummeting lines of frequency of searches. "The curves," he writes, "suggest that Americans are not just more abashed about confessing to prejudice than they used to be; they privately don't find it as amusing."

More optimistically, these declines in prejudice may be an underestimate, given that when Google began keeping records of searches in 2004 most Googlers were urban and young, who are known to be less prejudiced and bigoted than rural and older people, who adopted the search technology years later (when the bigoted search lines were in steep decline). Stephens-Davidowitz confirms that such intolerant searches are clustered in regions with older and less educated populations and that compared with national searches, those from retirement neighborhoods are seven times as likely to include "n*** jokes" and 30 times as likely to contain "fag jokes." Additionally, he found that someone who searches for "n***" is also likely to search for older-generation topics such as "Social Security" and "Frank Sinatra."

What these data show is that the moral arc may not be bending toward justice as smoothly upward as we would like. But as members of the Silent Generation (born 1925–1945) and Baby Boomers (born 1946–1964) are displaced by Gen Xers (born 1965–1980) and Millennials (born 1981–1996), and as populations continue shifting from rural to urban living, and as postsecondary education levels keep climbing, such prejudices should be on the wane. And the moral sphere will expand toward greater inclusiveness. SA

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Illustration by Izhar Cohen

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

This Book Stinks

A new volume has breaking news

By Steve Mirsky

Perhaps the most surprising thing to be found in the new book *Does It Fart? The Definitive Field Guide to Animal Flatulence* is that not all mammals do.

Dogs do—and often get blamed for it when they don't. Gorillas do, anywhere they want. Horses do, including the legendary thoroughbred Hoof Hearted, whose name took on new meaning when the track announcer made his excited call. Hyenas do, and it smells really bad, for reasons you can probably sniff out, after they've eaten camel intestines, according to the book. So I would have bet a box of baked beans that all us members of the class Mammalia shared this fetid feature. But sloths don't. And it's not that they do it so slowly nobody notices.

The gut flora of sloths produce methane from the animals' leafy diets—and lots of it. But as authors Dana Rabaiotti and Nick Caruso note, "it is absorbed through the gut and into the bloodstream before being breathed out." Yet another good reason why sloths should not light their own cigarettes.

Let's take a wind break to examine how this book bubbled into being. The author bios explain that Rabaiotti "is a zoologist currently studying the impact of climate change on African wild dogs ... at the Zoological Society of London." (Yes, African wild dogs fart.) She is also affiliated with University College London. Which is ironic, as that institution was home to scientists who discovered five noble gases.

Caruso "is an ecologist ... at the University of Alabama, where he studies the role of climate in population biology of Appalachian salamanders." We also learn that "while researching the various animals for this book, he has found a new appreciation for farts." (More research is necessary to determine if salamanders fart, as they "may not possess strong-enough sphincter muscles to create the necessary pressure for a definitive flatus.")

In the introduction, we read that one day Rabaiotti was asked by a relative if snakes farted. She realized she didn't know. So she contacted David Steen, a snake expert at Auburn University. He tweeted back at her, "<sigh, yes>." The sigh was because the question was actually quite common—which became obvious as scientists on Twitter revealed that they, too, had been queried as to the flatus status of their study animals.

Quickly awash in information, Caruso created the #DoesItFart hashtag, "and, in the true nature of science, this swiftly spawned a spreadsheet." Caruso and Rabaiotti chose 80 animals, expounded on these organisms and their gaseous habits, threw in some charming drawings by artist Ethan Kocak (whose work has appeared on the *Scientific American* Web site), and loosed *Does It Fart?* upon an unsuspecting world.

The answer to the title question for most entries is a resounding "yes." The very first critters considered, herring, include a couple of species that "have taken the art of farting to new depths." They gulp air at the water's surface, store it in swim bladders, and expel it from anal ducts in fast repetitive ticks (FRTs)—fart dots and dashes, which they may be using to communicate. Think Samuel Morse after an especially fiber-rich dinner.

A species of insect commonly known as the beaded lacewing produces larvae that stun and kill their termite prey (yes, by the way) by farting a chemical that induces paralysis. The authors don't mention if the fart is silent, but it's definitely deadly.

The entry for whales begins, "As you can imagine," which I'll let you do. Giraffe farts take place, according to the spreadsheet, "at 'face height' of the average man." But what merely average man would be right behind a giraffe? Skunks fart because it would be a cruel joke if they didn't.

The book does list a few noes, such as sea anemones, sea cucumbers, Portuguese man-of-wars (or is it men-of-war?), goldfish (unless they are having digestive issues), octopuses, soft-shelled clams and the 10,000 species of birds. Nevertheless, parrot owners have reported what sound like loud expulsions coming from their birds. But keep in mind that parrots are excellent mimics. SA

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Illustration by Matt Collins

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Live stream from New York and Oslo
Details and live stream on **www.kavliprize.org**

Since 2008, the Kavli Prize has been honoring scientists for their seminal research in **astrophysics, nanoscience and neuroscience.** Now watch as the 2018 Kavli Prize Laureates are announced live from Oslo, with a special program from New York.

The Kavli Prize awards $1 million in each of the three fields.

Laureates are chosen by international committees whose members are recommended by six of the world's most renowned science societies and academies.

The Kavli Prize is a partnership between **The Norwegian Academy of Science and Letters**, **The Kavli Foundation** (United States), and **The Norwegian Ministry of Education and Research**.

THE NORWEGIAN ACADEMY OF SCIENCE AND LETTERS

THE KAVLI FOUNDATION

Norwegian Ministry of Education and Research

What determines how we think, feel and act?

What sparks a memory, enables us to compose music or be sociable? The Kavli Prize for Neuroscience celebrates advances in understanding the exquisite workings of the nervous system.

LEVEL OF DETAIL

WHOLE ORGAN

2008
A SENSE OF PLACE AND PURPOSE
Identification of the molecular cues used by nerve cells to organize themselves within embryonic tissue to form complex 3-D brain and spinal cord structures.

NETWORKS

2014
PRECISION MAPPING
The discovery of specialized brain networks and cells that perform complex mental tasks such as attention, spatial awareness and planning.

CIRCUITS

2012
COORDINATION IS KEY
For determining how brain circuitry can control behaviors such as movement, eating, and habits.

NEURONS

2016
USE IT OR LOSE IT
Elucidation of the mechanisms that remodel nerve cell circuits throughout adulthood, to allow them to learn or recover from injury.

SYNAPSES

2010
RELEASE, REUSE, REFILL
The discovery that the rapid relay of signals relies on proteins that control the movement of bubble-like containers (vesicles) that carry chemicals across nerve endings.

KAVLI PRIZE WINNERS

NEUROSCIENCE

2016

Eve Marder | Michael M. Merzenich | Carla J. Shatz

2014

Brenda Milner | John O'Keefe | Marcus E. Raichle

2012

Cornelia Isabella Bargmann | Winfried Denk | Ann Martin Graybiel

2010

Richard H. Scheller | Thomas C. Südhof | James E. Rothman

2008

Pasko Rakic | Thomas Jessell | Sten Grillner

What is our place in the Universe?

The movements of the heavenly bodies have long inspired thinkers who have pondered the nature of the cosmos. Copernicus, Kepler, Galileo and Newton laid the foundations of modern astronomy, yet only in the 20th century did we begin to truly grasp the expanding vastness of space and diversity of its contents. The winners of the first five Kavli Prizes in Astrophysics have all contributed towards major leaps in our understanding of the Universe and our place within it.

EARTH

2010
TAKING THE LONG VIEW

The development of bigger, lighter, and more adaptable telescopes that have allowed astrophysicists to observe fainter, more distant phenomena.

SOLAR SYSTEM

2012
OUT IN THE COLD

The discovery that, beyond Neptune, in the outer reaches of the Solar System, lies the Kuiper Belt — a vast ring of millions of small icy objects.

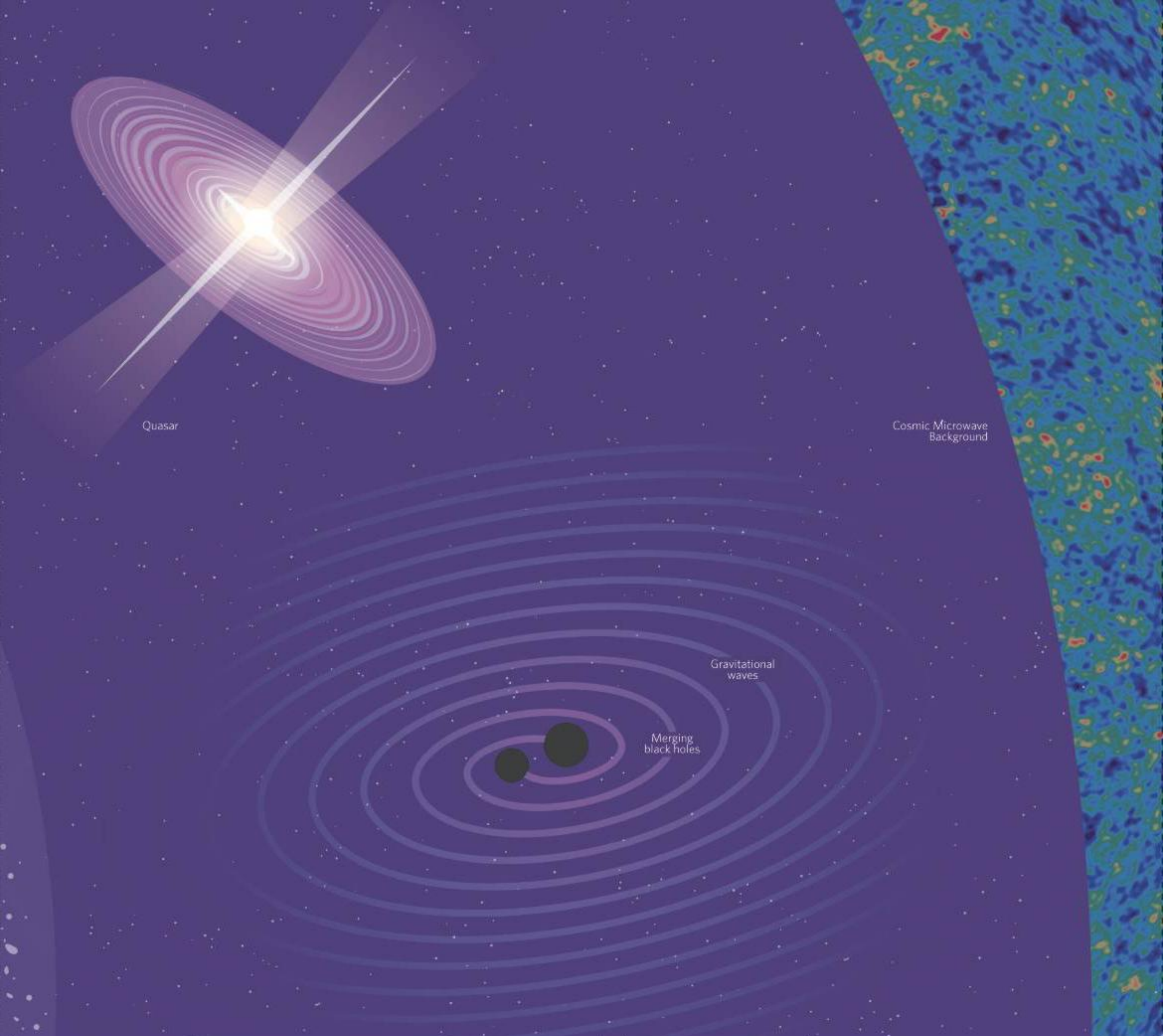
KAVLI PRIZE WINNERS
ASTROPHYSICS

2016

Ronald W.P. Drever — Kip S. Thorne — Rainer Weiss

2014

Alan H. Guth — Andrei D. Linde — Alexei A. Starobinsky



BEYOND THE MILKY WAY

EDGE OF THE UNIVERSE

2008
DISTANT DAZZLERS
The description of quasars, which emit immense amounts of electromagnetic radiation, including visible light and X-rays, thought to be generated as spiralling disks of gas and dust are sucked into supermassive black holes.

2016
THE BIG SQUEEZE
The detection by LIGO of ripples in space-time that squeeze and stretch things in their path, caused by the movements of distant objects, such as the merger of two black holes.

2014
GARGANTUAN GROWTH SPURT
The theory that the Universe underwent a brief period of exponential expansion immediately after the Big Bang, which helps explain its flatness and the uniformity of the cosmic microwave background.

2012


David C. Jewitt


Jane X. Luu


Michael Edwards Brown

2010

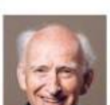

Jerry E. Nelson


Raymond N. Wilson


James Roger Prior Angel

2008


Maarten Schmidt


Donald Lynden-Bell

KAVLI PRIZE WINNERS
NANOSCIENCE

2016

Gerd Binnig · Christoph Gerber · Calvin Quate

2014

Thomas W. Ebbesen · Stefan W. Hell · Sir John B. Pendry

2012 · 2010

Mildred S. Dresselhaus · Donald M. Eigler · Nadrian C. Seeman

2008

Louis E. Brus · Sumio Iijima

10 YEARS OF PRIZES FOR THE FUTURE · THE KAVLI PRIZE 2008-2018 ·

How will the 2018 prizes deepen our understanding of our Universe? **Find out on 31 May at www.kavliprize.org**

What happens at the smallest scales?

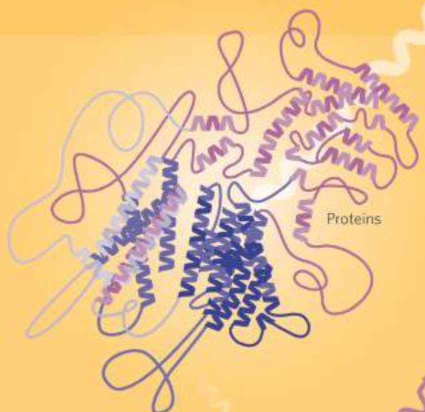
Pioneering researchers have expanded our understanding of the unique properties of materials at atomic and molecular scales, enabling a range of applications.

100 - 1,000 nanometers (nm)

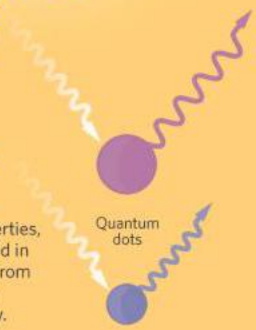
Abbe Diffraction Limit (~200 nm)

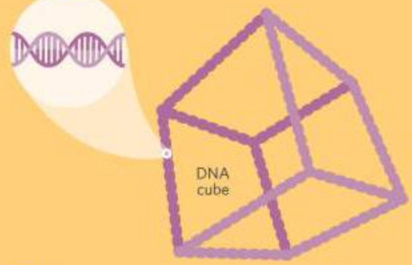
*The resolution of optical microscopes is limited to approximately half the wavelength of visible light.

10 - 100 nm



2014
BREAKING THE LIMIT
The invention of techniques that exploit quantum phenomena to image nano-sized objects and control light at unprecedented resolution.



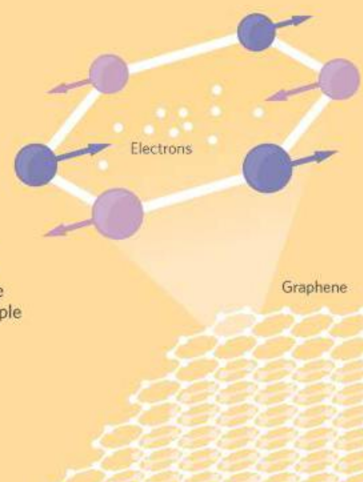


2008
CHANGING PERSPECTIVES
The discovery that nanostructures have size-dependent properties, which can be exploited in applications ranging from electronic displays to targeted drug delivery.

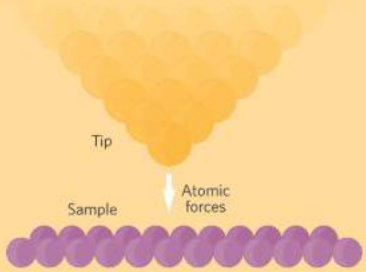
2010
FINE CONTROL
For the ability to manipulate atoms and molecules into structures, revealing details of fundamental physical properties of matter.

1 - 10 nm

2012
ENERGY FLOW
The discovery of the type of interaction between electrons and atomic vibrations in nanostructures, such as graphene, which can be engineered to harvest thermal energy more effectively.



2016
MEASURING ATOMS AND MOLECULES
Invention of atomic force microscopy, which utilizes the small force between the atoms and molecules in a sample and a very fine tip to image with atomic resolution.



50, 100 & 150 YEARS AGO

INNOVATION AND DISCOVERY AS CHRONICLED IN *SCIENTIFIC AMERICAN*

Compiled by Daniel C. Schlenoff

JUNE

1968 The Politics of Riots

"A view of the U.S. urban riots of the past four years as a 'prepolitical' form of collective action rather than a series of senseless outbreaks of blind rage is beginning to emerge among social scientists. While there is no consensus among investigators, all of whom agree that the riots have varied and complex origins, there is general emphasis on the idea that the disorders represent more than a Negro protest, more than a sudden reaction to years of deprivation. The riots are seen rather as implicitly political demonstrations, although not as organized, conspiratorial political acts. This view is illustrated by a number of papers on urban violence and disorder in a recent issue of the *American Behavioral Scientist*. 'Rioting evolves as a form of collective pressure or protest where large numbers of people are crowded and alienated together, sharing a common fate that they no longer accept as necessary.'"

Daily Bread

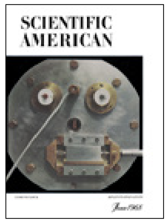
"The disappearance of stones in the urinary tract is particularly well documented in England. Between 1772 and 1816 one in every 38 patients at the Norfolk and Norwich Hospital was under treatment for bladder stones. In the same period so many of the boys at the Westminster School in London suffered from bladder stones that they had their own hospital ward. A factor that may be related to the decline of stones, Dame Kathleen Lonsdale of University College London suggests, is that the bread the English ate during the 19th century was heavily adulterated with alum and chalk."

1918 Raising the Alarm

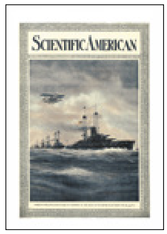
"An organization of automobile owners in London has rendered valuable service to the public in connection with the raids of the German air pirates. When warning of an air raid is received in the city, explosive sky rockets are fired from various points. As depicted on our cover this week, the automobiles then drive through the city streets, honking their horns to attract attention. On each side of the car, a large sign is carried, on which is printed the warning, 'Take Cover.' When the danger is passed the reverse side of the sign is shown, which reads, 'All Clear.' A Boy Scout bugler who rides in the car also assists to inform the citizens that the Huns have departed."

1868 Visiting Vesuvius

"At a recent meeting of the Royal Institution, Professor Tyndall was invited to state what he saw during his recent visit to Vesuvius. The country all round Naples is very smoking and hot, showing the existence of extensive subterranean fires. He also explored some hot subterranean galleries in the side of the mountain, and visited the Grotto del Cano, the well-known cavern, where the floor is covered several feet deep with carbonic acid gas [carbon dioxide]. The heavy invisible gas, in fact, runs out of the cavern in a great stream, and will in the open air put out torches when they are held near the ground. A little dog is kept near the cave to be half suffocated by immersion in the gas when visitors arrive; and Professor Tyndall protested against the cruelty of the experiment, which, he says, serves no useful purpose, and ought to be stopped."



1968



1918

1868

1918: A Boy Scout helps to warn civilians in London to take cover during an air raid.

SCIENTIFIC AMERICAN, VOL. CXVIII, NO. 23; JUNE 8, 1918

The Dust Bin

"There is not one particle in the heap the scavenger removes from our houses that is not again, and that speedily, put into circulation and profitably employed. No sooner is the dust conveyed to the yard of the contractor than it is attacked by what are called the 'hill women,' who, sieve in hand, do mechanically what the savant does chemically in his laboratory, separate the mass, by a rude analysis, into its elements. The most valuable of these items are the waste pieces of coal, and what is termed the 'breeze,' or coal dust and half-burnt ashes. The amount of waste that goes on in London households in this item of coal can hardly be conceived."

Médecine Moderne

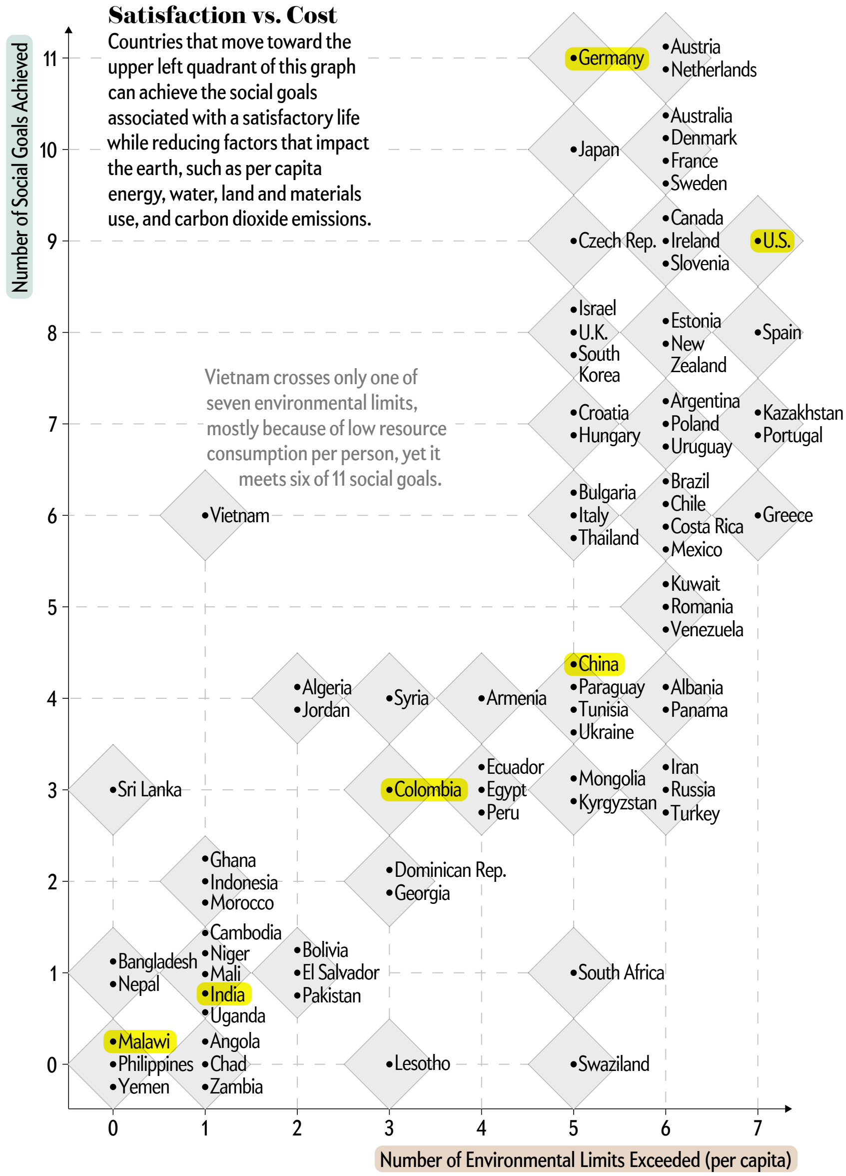
"The use of raw meat in the treatment of debility and consumption is in the ascendant in France: but that it may be served in a style the least objectionable to the patient's delicate sensibilities, it is prepared under the name of musculine tablets, and is made of raw fillets of beef covered with fruit jelly and candied sugar."

Text by Mark Fischetti | Graphic by Federica Fragapane

A Good Life for All

Can humans live well without pillaging the planet?

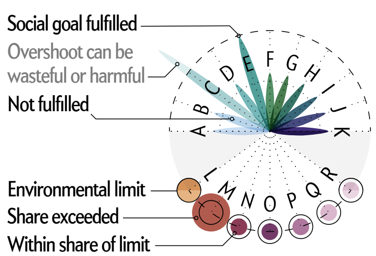
Many wealthy nations achieve a range of social objectives that together can provide a good life for their people, as outlined by the United Nations Sustainable Development Goals. But to do so, they exceed their share of the earth's natural resources and surpass environmental impact limits needed to safeguard the planet, according to a recent study (*top right of main graph*). Less wealthy nations use resources more modestly and have lower impacts but meet fewer of the social goals (*bottom left of main graph*). The solution: "Wealthy nations can consume less, with no loss in quality of life," says study leader Daniel W. O'Neill of the University of Leeds in England. That would free up resources for less wealthy nations to improve lives (*circular charts*) while still keeping within safe environmental boundaries.



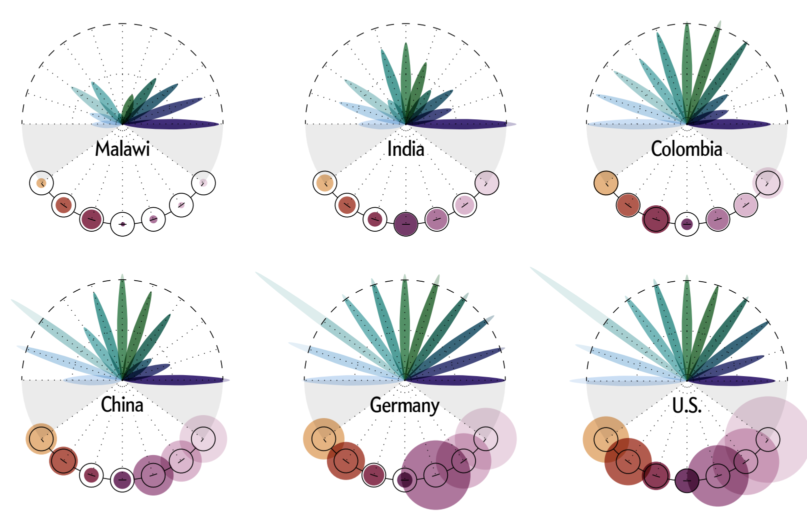
Satisfaction vs. Cost
Countries that move toward the upper left quadrant of this graph can achieve the social goals associated with a satisfactory life while reducing factors that impact the earth, such as per capita energy, water, land and materials use, and carbon dioxide emissions.

Country Goals and Limits

Social Goals
- A Life satisfaction
- B Years of healthy life
- C Nutrition
- D Sanitation
- E Sufficient income
- F Access to energy
- G Education
- H Social support
- I Democratic rights
- J Income equality
- K Employment rate



Environmental Limits
- L Materials use
- M Land and ocean use
- N Crop and forest loss
- O Freshwater use
- P Nitrogen discharge
- Q Phosphorus discharge
- R CO_2 emissions



SOURCE: "A GOOD LIFE FOR ALL WITHIN PLANETARY BOUNDARIES," BY DANIEL W. O'NEILL ET AL., IN *NATURE SUSTAINABILITY*, VOL. 1; FEBRUARY 5, 2018 *https://goodlife.leeds.ac.uk*