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ROUGH WEATHER AHEAD
Yes, climate change is making storms worse PAGE 46

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life

Uncovering the Origins of Evolution's Big Bang

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Can one shot prevent many diseases? PAGE 54

JUNE 2019
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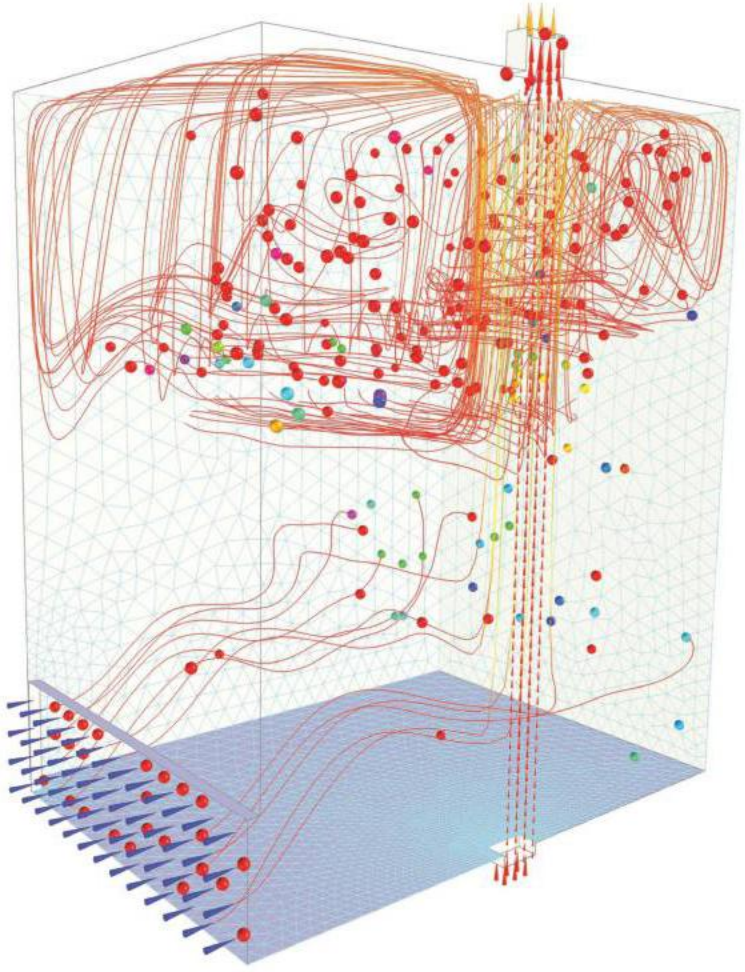
Prevent epidemic outbreaks with mathematical modeling and simulation.



Visualization of the motion of bacteria particles in a room with a displacement ventilation system.

Using math to analyze the spread of epidemic diseases is not a new concept. One of the first compartmental models of mathematical epidemiology dates back to 1760 and was presented by Daniel Bernoulli for studying the mortality rate of smallpox. Today, medical researchers and public health officials continue to use mathematical modeling and simulation to prevent and control epidemic outbreaks in the modern world.

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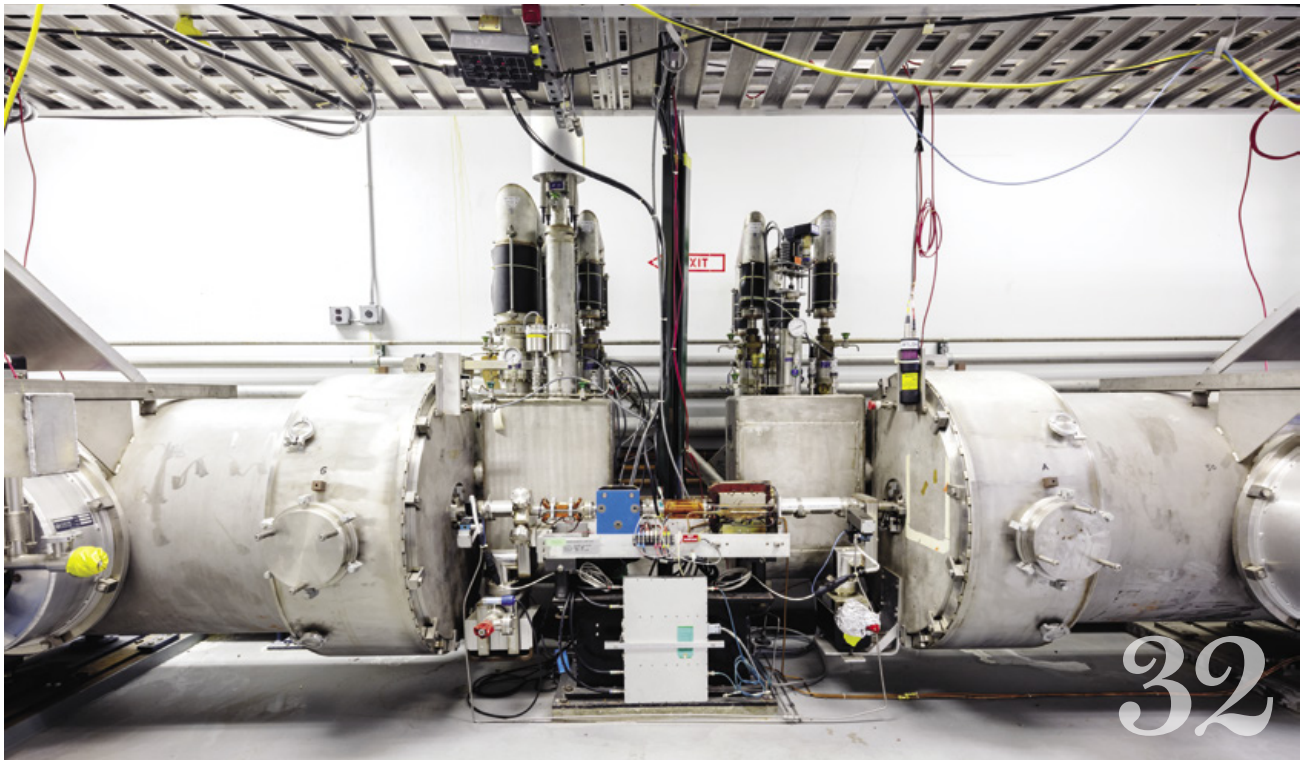

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New fossils and analyses of ancient ocean chemistry reveal the surprisingly deep roots of evolution's big bang—the Cambrian explosion. *By Rachel A. Wood*

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The fossil record shows that animal evolution was ramping up millions of years before the Cambrian explosion. Creatures from the preceding Ediacaran period were already evolving into predators, making protective skeletons and forming reef ecosystems, among other developments that preceded Cambrian diversification. **Illustration by Franz Anthony.**

Photograph by Floto + Warner

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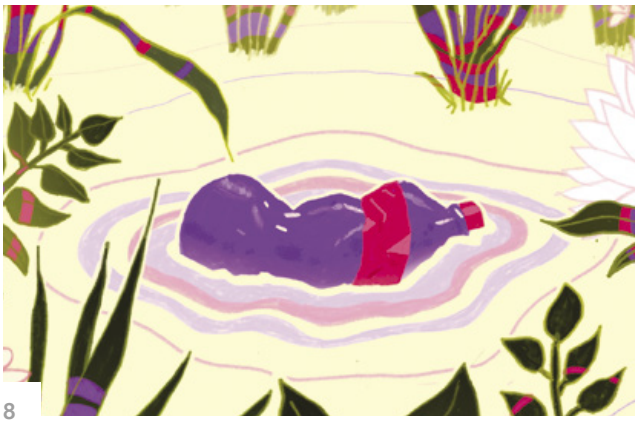
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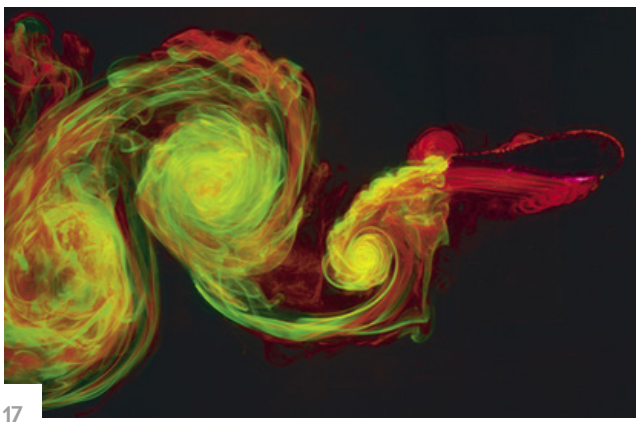
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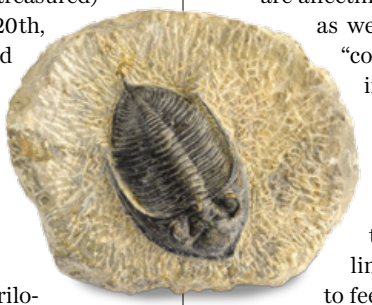
Mariette DiChristina is editor in chief of *Scientific American*. Follow her on Twitter @mdichristina

Understanding through Time

For fun, my husband and I have always followed the traditional themes for gifts marking significant wedding anniversaries, starting with paper, when he gave me a (still treasured) subscription to the *New York Times*. On our 20th, I was at first stumped by "china." We already had plates. Maybe, I thought, I could focus on the place rather than porcelain? Horizons opened, and I settled on bestowing on him a 380-million-year-old former denizen of China: a fossil trilobite. My husband was delighted; we both enjoyed reflecting on the symbolism of the arthropod's enduring journey on the earth.



Complex multicellular organisms such as trilobites burst onto the scene during the Cambrian explosion, starting 540 million years ago. The unevenness of fossilization, weathering and other processes, however, have made it difficult to see to the roots of these life-forms. Recent discoveries in Siberia, Namibia and other places are now showing that complex animals actually got their start millions of years before the Cambrian period. As geoscientist Rachel A. Wood of the University of Edinburgh writes in her cover story, "The Rise of Animals," new geochemical techniques are also helping us understand why Cambrian fossils emerged when they did. Dive in to page 24 to join Wood in her tale about how she and other researchers are gaining a deeper appreciation of these ancient epochs.

Time's a-wasting, as the saying goes, for action on climate change today, as will become obvious when you read "Rough Weather Ahead," by Jennifer Francis of the Woods Hole Research Center in Falmouth, Mass. Specific extreme weather events are worsened by climate change, scientists can now show. More heat in the ocean and more heat and vapor in the atmosphere are affecting weather globally. Regional effects play roles as well, including an expanding tropical zone, a "cold blob" in the Atlantic Ocean and disruptions in the polar vortex. Make haste to page 46.

Theories—in the scientific sense, explanations for observational evidence—around evolution and climate change have been met with skepticism in certain circles. Vaccines, thanks to a paper retracted years ago claiming a false link to autism, have also had critics. It's tempting to feel superior to the unconvinced, given the long-standing supporting evidence that documents how life evolves through random mutations and natural selection; anthropogenic activities are shifting the climate; and inoculations prevent disease without causing autism.

The process of research, as rational as it is, can nonetheless take time to clarify any given question. In "Vaccines Reimagined," starting on page 54, contributing editor Melinda Wenner Moyer looks at the controversial idea that one immunization, given properly, can protect against many diseases besides its target. Is it right? Only time will tell. SA

GETTY IMAGES

Illustration by Nick Higgins

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VIRTUAL HEALING

Thank you for "The Promise of Virtual Reality" [The Science of Health], Claudia Wallis's excellent piece on the uses of the technology in medicine. I would like to insert "medical education" as another potential tool for VR. My colleagues and I have published some research on using immersive VR to teach cardiac anatomy to medical students in the March issue of *Clinical Anatomy*. We found that they not only scored 24 percent higher on quizzes than non-VR students but also said they had "fun"! Fun should not be a dirty word in medical education.

Hillel S. Maresky *University of Toronto*

Wallis is excited about the completion of a randomized controlled trial on the use of VR to treat post-traumatic stress disorder. The problem is that you can't truly single-blind a VR trial and have the trial's subjects unaware whether they are receiving the treatment or a placebo, and the bias of knowing thus cannot be filtered. Stating that VR "will help make mental health care cheaper and more accessible" risks overselling an intervention that cannot be robustly validated.

Douglas Berger *Tokyo*

GEOSCIENCE GEOMETRY

"Is Antarctica Collapsing?" by Richard B. Alley, claims that a complete collapse of the Thwaites Glacier in West Antarctica could lead to a sea-level rise of 11 feet. I am puzzled because I cannot make the arithmetic work out.

Let's call Alley's figure 3.5 meters. For simplicity, let's also say a kilometer is 1/10,000 the distance from the pole to the equator, as it was originally defined. So the earth's circumference is 40,000 km, and its radius is about 6,400 km, giving a surface area of about 510 million square km. But the ocean is only about 70 percent of the earth's surface, or about 360 million km^2. (When I had a chance, I Googled it and confirmed my number.)

From the map, the glacier appears to be approximately a right triangle with each side measuring about 600 km. So its area is about 180,000 km^2. I assume only the portion above sea level matters. The article says the glacier rises up to a mile (1.6 km) above sea level, but clearly it is not that high everywhere, such as the coast, so let's guess 1.5 km on average. My rough estimate of the volume of the glacier above sea level is therefore 270,000 km^3. Ignoring the additional water necessary to shrink the coastlines as sea level rises, that is only enough water to raise sea level by, at most, about 0.7 meter.

I didn't expect my computation to be exact, but that results appears to be off by a factor of five. Did I do something wrong?

Dan Graifer *via e-mail*

ALLEY REPLIES: Graifer's math is pretty good. But West Antarctica is now drained by ice that flows in other directions, into the Ross and Filchner-Ronne ice shelves, as well as Thwaites, with so-called continental divides along the highest parts of the Antarctic Ice Sheet separating the different drainages. If Thwaites deglaciated to the divides and stopped there, it would leave mile-high cliffs that would not be stable. Both our physical understanding and our models show that deglaciating any of the main drainages of West Antarctica would tap into ice that now goes out the other drainages, deglaciating the marine basins of all of them. The total is usually taken to give us 3.3 meters, or 11 feet, of global sea-level rise without too much uncertainty.

"Fun should not be a dirty word in medical education."

HILLEL S. MARESKY *UNIVERSITY OF TORONTO*

PLANETARY PARITY

"The Exoplanet Next Door," by M. Darby Dyar, Suzanne E. Smrekar and Stephen R. Kane, states that Venus has no magnetic field and yet has an atmosphere of extreme density and depth. Mars, on the other hand, has almost no atmosphere. The explanation for the latter's thin atmosphere that I am most familiar with is that because the planet lost a strong magnetic field, the solar wind from the sun stripped it of a previously much thicker atmosphere.

I would think that Venus, being much closer to the sun, should have experienced a much greater solar wind effect. The two planets were created around the same time, so the atmospheric difference seems to defy common sense. What am I missing here?

Chris Scholfield *via e-mail*

THE AUTHORS REPLY: The key to answering this question is that Venus has a negligible magnetic field at the present epoch. We must not fall into the trap of thinking that this situation has persisted for the past four billion years. Assuming a composition and core size similar to Earth, models of the Venusian magnetic field through time show that the planet most likely had a field comparable to Earth's up until about one billion years ago. Crucially, this would have protected the Venusian atmosphere when the sun was younger and much more active. Additionally, Venus's atmosphere is much thicker and has a higher mean molecular weight than Earth's, which makes it generally more resistant to atmospheric escape degradation.

But exactly how magnetic fields shield atmospheres is apparently more complicated than once thought. For example, recent measurements suggest that oxygen is currently being lost from Earth, Mars and Venus at similar rates! This is a very puzzling result, given the idea that mass, magnetic field and distance from the sun are the main factors in atmospheric loss, as Scholfield notes.

A HEAD FOR FACES

In "Face Values," Doris Y. Tsao describes a technique in which she and her colleagues are able to predict how neurons in certain areas of the cerebral cortex that are dedicated to facial recognition will respond to a given face by using 50 coordinates, or dimensions, for shape and appearance.

One intriguing piece of information absent from the article is the number of discernible steps along the ramps from minimal to maximal neuron cell response. To illustrate: If only nil and maximum values could be distinguished for each coordinate, then for a 50-D space, there would be about 10^{15} distinct facial states. This seems likely to be more than the number of individuals who would be recognizable to a single person and raises the question of why this seemingly excessive capacity is produced by evolution of the visual sense.

TERRY GOLDMAN
Los Alamos National Laboratory

TSAO REPLIES: Relating the noise characteristics of face neurons to facial discrimination behavior is an interesting idea. I'm not sure there is a discrepancy between the number of neurally distinguishable states and our ability to perceive them: as the existence of the plastic surgery industry demonstrates, we can distinguish very fine differences in facial structure.

Why the brain evolved to represent faces based on these shape and appearance axes is a deep and open question. One idea is that the fundamental job of the brain is to build an efficient model of the world—rather than to accomplish ad hoc goals such as distinguishing the faces of people you know—and extracting shape and appearance parameters is the best way to do this in the realm of face modeling. What we do know is that with 50 numbers describing shape and appearance, we can recreate a face.

ERRATUM

"Is Antarctica Collapsing?" by Richard B. Alley, should have referred to the National Science Foundation launching an effort to study the Thwaites Glacier with the U.K.'s Natural Environment Research Council, not the British Antarctic Survey.

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What to Do about Plastic Pollution

Bans on bags will not solve a global recycling failure

By the Editors

From the bags that find their way to the ocean and into the stomachs of whales to the straws that hurt turtles to the microscopic shards and synthetic fibers that have been found in the remote Arctic, plastic permeates the planet.

The problem of plastic pollution has gotten dramatically worse as production has ramped up from two million metric tons a year in 1950 to more than 300 million metric tons a year today without much thought to what happens once it is discarded. The thousands of polymers that fall under the catchall label "plastics" never disappear. They merely degrade into smaller pieces called microplastic. A 2017 study in *Science Advances* estimated that of all the plastic ever produced, 90 percent is still around, mainly in landfills or out in the environment (the rest has been incinerated). Bans on single-use plastic such as bags and straws have become a popular policy around the world to rein in plastic use. But although some of these rules have reduced waste in places, including Ireland and California, they do not directly address production and can send users to alternatives that are not much friendlier to the environment.

Researchers have learned enough about the flow of plastic waste to know it poses a widespread environmental problem. Plastic causes physical harm to animals and could combine with other threats to endanger vulnerable species. There is also concern about humans inhaling and ingesting microplastic. We must do a better job of stanching the flood. Doing that means tackling two broad goals: considerably reducing the amount of plastic we produce and improving the recycling and reuse of what we make.

The U.S. must be a bigger part of these solutions. Blame is too often laid solely at the feet of rapidly developing Asian countries that lack robust waste-management systems, and we forget the role that the U.S. plays not only in producing plastic but by exporting millions of tons of the waste to Asia. With China no longer accepting imports of much recyclable waste, it has forced a reckoning in the U.S., with the local authorities responsible for an overwhelmed recycling system turning to landfills and incinerators. Those options can have other environmental impacts and perpetuate the creation of virgin plastic from fossil fuels, instead of reusing and recycling existing plastic. Only 9 percent of plastic in the U.S. is now recycled, according to the Environmental Protection Agency.

Federal and state governments should step up to help streamline and shore up the nation's disjointed recycling system. This could be done, for example, by standardizing what can be recycled and putting limits on additives such as coloring, which is expensive to remove and can make plastic less valuable to a recycler. Governments could also fund recycling and composting infrastructure in communities that otherwise might not be able to afford it. Such investments could spur American innovation in the area, for example, setting the stage for wider use of compostable plastic, which can currently only be properly broken down in industrial facilities.

Many researchers also say plastic product manufacturers need to be pushed beyond their present voluntary commitments to reduce plastic waste with incentives that will make them bear more of the cost of that waste. Countries from the U.K. to India are looking at such "extended producer responsibility" programs, which can include taxes on new products that do not have a certain percentage of recycled plastic, along with having producers pay toward the costs of collecting and recycling their products.

Each policy has its proponents and detractors, and it is ultimately up to lawmakers to decide which ones make the most scientific, economic and political sense. In the U.S., Congress has already shown it is willing to step in, with the 2015 Microbead-Free Waters Act that banned these infinitesimally small materials in personal care products. A planned update to the bipartisan 2018 Save Our Seas Act, aimed at dealing with marine debris, could call for neutral arbiters such as the Congressional Research Service and the National Academy of Sciences to evaluate the costs and efficacy of various policies to make sure that the solutions we pursue do not create unintended consequences.

We need comprehensive solutions, not just Band-Aids that cover up the symptoms but ignore the roots of the plastic problem. SA

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Illustration by Skip Sterling

Katie Mehnert is founder of Pink Petro and Experience Energy. She testified before the House Committee on Energy & Commerce's Subcommittee on Energy on February 27, 2019.

More Women = Better Energy

Diversity leads to innovation, which is crucial to fight climate change

By Katie Mehnert

Climate change is one of the most monumental challenges of our time. But even as it draws increasing calls for action, one of the most important steps we can take still gets far too little attention: we need more women in the energy sector. Only 15 percent of employees in the oil and gas industry are women, and that number is even smaller when you look at higher-paying technical jobs.

Despite popular belief to the contrary, most leaders in oil and gas do recognize the reality of climate change. And many say they want to do something about it. A survey by Ernst & Young (EY) found that 93 percent of oil and gas executives believe climate change is real, and 67 percent say oil and gas companies want to and can be part of the solution.

I think these figures—and the industry's actual commitment to reducing emissions—would increase further if there were more women executives at these companies. The Yale Program on Climate Change Communication recently reported that "on average, women are slightly more likely than men to be concerned about the environment and have stronger pro-climate opinions and beliefs." And for years some women in energy fields have been prominent voices calling for greater action.

To implement that action, the oil and gas industry also needs *innovation*. It needs a constant influx of new ideas, systems, technologies and business structures. The EY survey found that only 37 percent of oil and gas executives believe their companies are currently doing a good job combating climate change. Innovation could change that trend, and more women would bring it. As the *Stanford Social Innovation Review* has reported, growing evidence shows that greater equality breeds innovation—"the creation of new and potentially disruptive ideas, products, or services."

This is true for all forms of diversity. The more different perspectives and life experiences that people bring to boardrooms and work teams, the more innovative ideas they can come up with together.

I see this in action every day—and I see how far the traditional energy sector has to go. It was just a few years ago that a man I sat next to on a flight asked me, "What's a pretty young lady like you doing in a dark, dangerous business like oil and gas?" Comments like that are one reason I left a career in big oil to launch my own company aimed at bringing more women into the business. There are still far too many obstacles preventing women from entering the energy field and from reaching their full potential within it.

The sector is paying a deep price for its long-term failure to recruit and retain a diverse workforce. When other industries beefed up operations to establish talent pipelines into diverse communities, far too many energy companies did not.

We also need stronger STEM programs for young women and ample support for those programs from the oil and gas companies. My organization, Pink Petro, included these steps and more in a report listing recommendations to close the gender gap in oil and gas. And I launched Experience Energy to help energy companies and talented female candidates find each other.

To move forward, oil and gas companies also need to erase the negative perceptions many people have of the industry. As EY describes, for instance, its survey found that "less than a quarter of consumers believe most oil and gas companies have acknowledged that climate change is real." The industry is aware it needs to improve its communication with the public and awareness of its efforts to protect the environment.

My husband, daughter and I have witnessed the devastation of climate change firsthand in Houston. We lost our home and my business during Hurricane Harvey. In our city, the energy capital of the world, most conversations around climate change revolve around big questions—a growing search for new ideas and a desire to transition into new ways of operating. We talk a lot about how our most important resource is the workforce that can power us forward.

For big ideas to flourish and big actions to follow, people of all backgrounds must be at the table tackling these challenges together. It is time all Americans see themselves represented among the decision makers at the companies that fuel our world. SA

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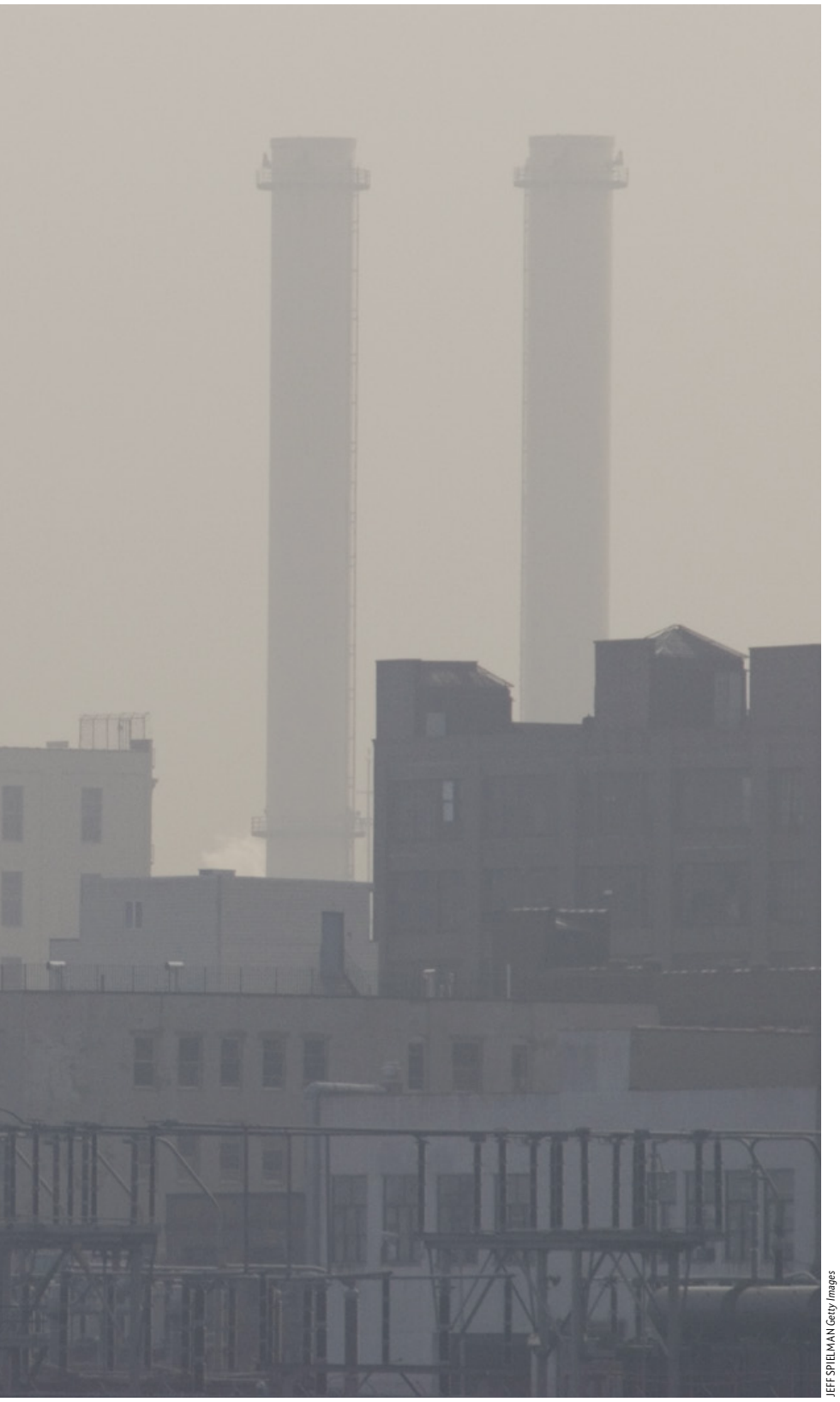
Illustration by Tara Jacoby

ADVANCES

Pollution, like that in this neighborhood in Brooklyn, affects racial groups unequally.



JEFF SPIELMAN *Getty Images*

INSIDE

- Brainy slime molds can make complex decisions
- Cats know their names, even if they ignore them
- Simulating how speedy wings evolve
- An "Internet of plants" could provide real-time agricultural monitoring

PUBLIC HEALTH

Air Inequality

U.S. racial minorities are exposed to more air pollution than white people yet cause less of it

Harlem and the South Bronx have some of the highest asthma rates in New York City. And these predominantly black and Hispanic neighborhoods—studded with smokestacks and crisscrossed by gridlocked highways—are emblematic of a large body of research showing clear racial disparities in exposure to air pollution.

A study published in March in the *Proceedings of the National Academy of Sciences USA* shows that even though black and Hispanic people in the U.S. are exposed to more air pollution than white people, these groups consume less from the industries generating much of that pollution. The findings put hard data behind inequities that environmental justice advocates have reported on the ground, revealing that racial minorities bear a disproportionate amount of the costs of emissions tied to higher levels of consumption. "It echoes things we've been saying for decades in the environmental justice movement," says Kerene N. Tayloe, director of federal legislative affairs at nonprofit WE ACT for Environmental Justice.

The study also found that these disparities persist despite substantial overall reductions in air pollution in recent decades. Robert Bullard, a professor of urban planning and environmental policy at Texas Southern University, who was not involved with the

work, says this finding underscores the need to craft policies that reduce such pollution in the hardest-hit communities.

The researchers focused on fine particulate matter with a diameter of 2.5 microns or less ($PM_{2.5}$), generated by construction, fires and the combustion of fossil fuels. These particles can contain hundreds of different chemicals and can penetrate deep into the lungs, contributing to heart and lung disease. As part of its study, the team estimated that 102,000 people die prematurely every year from $PM_{2.5}$ emissions from human-made sources (as opposed to wildfires or other natural sources). That number is nearly double the amount of people who die annually from car crashes and murders combined, says study co-author Jason Hill, a biosystems engineer at the University of Minnesota.

To trace exposure back to the root cause of emissions, the investigators mined publicly available economic and $PM_{2.5}$ data. They linked emissions from various sources (such as coal-fired power plants or diesel vehicles) to economic activity that largely drives these emissions (such as electricity use or food purchases). Next they apportioned this consumption among racial groups and found stark disparities: on average, black and Hispanic people are exposed to 56 and 63 percent more $PM_{2.5}$, respectively, than the amount generated by their consumption, whereas white individuals are exposed to 17 percent less (*graphic*). "It's a pretty dramatic difference," Hill says.

The analysis made clear that a wide range of economic activity contributes to $PM_{2.5}$ exposure. It also showed that the higher relative contribution from white people was not the result of buying more from highly polluting sectors but rather of higher overall consumption. Household income was a factor in the observed differences, but it did not account for the entire mismatch.

Even though the total number of deaths from $PM_{2.5}$ exposure has declined in recent years, most likely because of regulations, the idea "that everyone is receiving the same level of protection is blown away" by the new findings, Bullard says. The results from this study, he adds, emphasize the need to undo the legacy of previous policies and decisions that placed polluting infrastructure disproportionately in low-income and minority communities. "How can we somehow change this paradigm that it's okay to keep polluting communities of color and communities that have contributed least?" Bullard asks. Hill says authorities cannot simply target any one category of emitter, such as coal-powered plants or diesel vehicles; all the involved industries must be addressed.

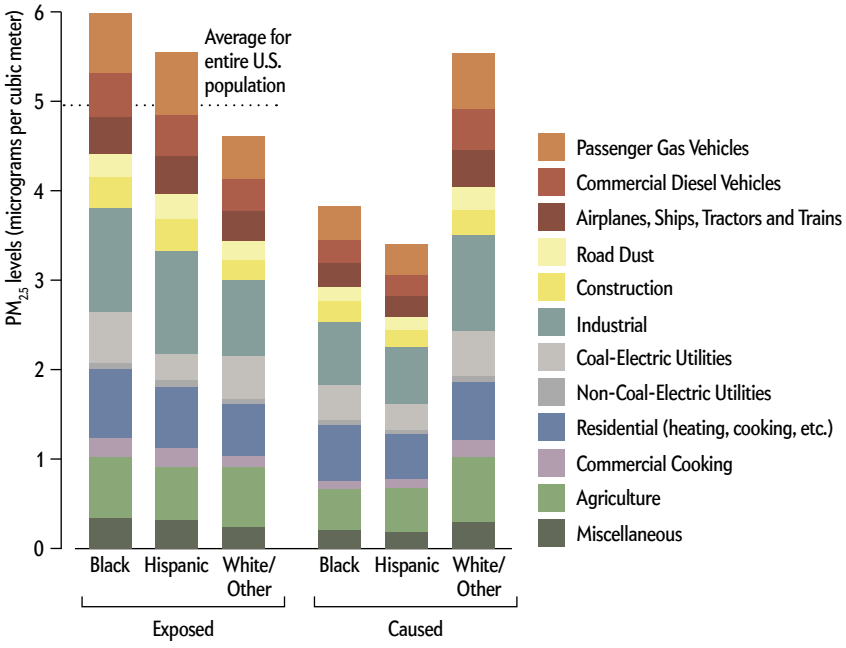
Scientists, legislators and communities will need to jointly work out which policies and regulations can tackle overall pollution while reducing these inequities, Hill and others say. This new framework for tracking pollution exposure provides a tool to do that, says Anjum Hajat, an epidemiologist at the University of Washington School of Public Health, who was not involved with the research. It could, she says, be used to evaluate how regulations targeting certain air pollution sources actually reduce exposure for various groups—and could also potentially reveal any unintended consequences, such as shifting pollution to other areas.

The work also underscores how important existing air pollution regulations are at a time when the Trump administration has moved to roll back several of them, including some governing pollution from coal-fired power plants and fuel efficiency in vehicles. When reached for comment, an Environmental Protection Agency spokesperson said the agency "will continue to monitor and report on key environmental indicators in low-income communities as a part of our commitment to healthy air, water and land for all Americans."

Research shows that even low levels of $PM_{2.5}$ can be harmful to the most vulnerable groups, such as children with asthma, so officials should be ratcheting up efforts instead of backing off, Hajat says. "We have seen this decline in [overall] air pollution over time" even as consumption has increased, she says, "so imagine what could happen if we really did make an effort as a society." —*Andrea Thompson*

Racial Groups' Exposure vs. Contribution to Air Pollution

Black and Hispanic individuals in the U.S. are exposed to higher levels of fine particulate matter ($PM_{2.5}$), on average, than white individuals yet consume less of the goods and services that cause such pollution. Black people, on average, experience the highest absolute pollution levels of the groups studied, whereas Hispanic people are exposed to the highest levels relative to their consumption.



SOURCE: "INEQUITY IN CONSUMPTION OF GOODS AND SERVICES ADDS TO RACIAL–ETHNIC DISPARITIES IN AIR POLLUTION EXPOSURE," BY CHRISTOPHER W. TESSUM ET AL., IN *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES USA*, VOL. 116, NO. 13: MARCH 26, 2019

Every year an estimated 102,000 people die from human-caused $PM_{2.5}$ pollution.

Graphic by Melissa Thomas Baum, Buckyball Design

IN THE NEWS

Quick Hits

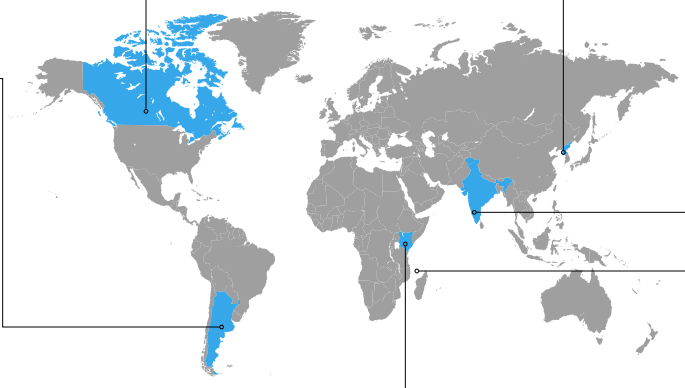
By Jim Daley

CANADA

Archaeologists have now confirmed that a *Tyrannosaurus rex* skeleton found in the 1990s at a fossil site in Saskatchewan is the biggest and heaviest on record. At nearly 42 feet long and almost 20,000 pounds, "Scotty" surpassed the record set by "Sue," which was found in South Dakota in 1990.

NORTH KOREA

Physicists at Kim Il Sung University in Pyongyang have brokered a rare agreement to collaborate with Italy's International School for Advanced Studies in Trieste. The North Koreans will study computational neuroscience with Italian physicists.



ARGENTINA

Archaeologists identified a site where ancient humans killed and butchered giant ground sloths (*Megatherium americanum*) in the Pampas region in eastern Argentina. The find provides evidence that humans contributed to the sloths' extinction.

INDIA

Biologists discovered a new frog species, which is an inch long, brown and speckled with blue dots. *Astrobatrachus kurichiyana*, dubbed the "starry dwarf frog," is found in the Western Ghats Mountains.

COMOROS

Geochemists at Columbia University found a lode of quartzite, a metamorphic rock formed from sandstone, on the Indian Ocean island of Anjouan. The island is volcanic and had been thought to contain only igneous rocks.

KENYA

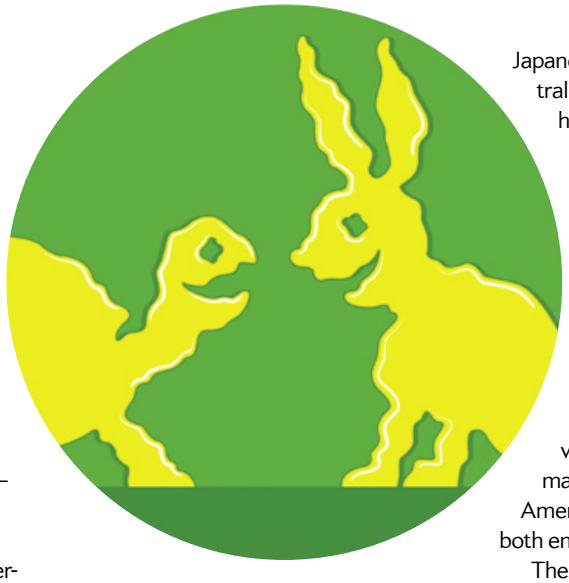
A science teacher who won the 2019 Global Teacher Prize announced he intends to donate the $1-million award to benefit society. Peter Tabichi, a Franciscan friar, mentors a science club that came in first in its category in the 2018 Kenya Science and Engineering Fair.

For more details, visit www.ScientificAmerican.com/jun2019/advances

BEHAVIORAL BIOLOGY

Slimy Smarts

Slime molds engage in complex, varied decision-making



In the film *The Wizard of Oz,* the scarecrow famously pines for a brain but eventually comes to realize that he already possesses all the smarts he needs. Similarly, acellular slime molds—strange, gelatinous organisms that consist of a single cell with billions of nuclei—lack a brain yet sometimes act like far more sophisticated creatures.

"We can't say that slime molds have personalities, because people would be very upset," says Audrey Dussutour, a behavioral biologist at Toulouse University III–Paul Sabatier in France. But "these giant cells have quite complex behaviors and display different ways of making a decision."

Dussutour and her colleagues were interested in studying how three strains of a particular slime mold species handle trade-offs between speed and accuracy when trying to find food. After presenting strains native to Japan, Australia and the U.S. with food sources of varying quality, the researchers observed which ones the organisms chose to engulf and consume. The Japanese strain acted quickest, randomly selecting whatever food it found. The Australian strain took longest but typically chose the best food. The American slime mold decided more slowly than the Japanese strain but faster than the Australian one and also opted for the highest-quality grub.

The speedy Japanese slime mold would likely have an edge in places where resources are scarce and competition is high, making any food better than no food, the researchers reported in February in the *Proceedings of the Royal Society B.* The Australian strain might be better suited to resource-rich environments in which slow decision-making would maximize nutritional benefits. The American strain would probably thrive in both environments.

These findings add an ecological spin to the growing body of work on decision-making capabilities in the simplest organisms, says James Marshall, a theoretical and computational biologist at the University of Sheffield in England, who was not involved in the study. "Taking longer over making the right decision can make sense in isolation, but when competing with others, being quick but inaccurate can be better."

—Rachel Nuwer

Illustration by Thomas Fuchs

BIOTECH

Sonic Therapy

Ultrasound stimulation through skin could treat inflammation

Ultrasound is used widely in medical imaging, but in recent years scientists have started honing it for another use: stimulating nerves to treat disease. In two new studies in rodents, researchers focused the sonic vibrations on nerves in the spleen that communicate with the immune system, reducing inflammation. If the approach proves safe and effective in people, it could serve as a noninvasive treatment for inflammatory diseases such as rheumatoid arthritis.

About 20 years ago neuroscientist Kevin Tracey and his colleagues discovered that brain signals traveling along the vagus nerve exert control over the immune system. "These [signals] are primitive reflexes that arise in the brain stem, evolved to preserve the integrity and health of cells in the body," says Tracey, president and CEO of the Feinstein Institute for Medical Research in Manhasset, N.Y. Stimulating the nerve is a way to hack into those reflexes.

The vagus nerve consists of a bundle of fibers that branch into many organs. It connects with the immune system via a second nerve that innervates the spleen, where circulating immune cells make a stop before flooding the bloodstream again. The new studies, published in March in *Nature Communications,* suggest that sending ultrasound to the spleens of mice through their skin may hit the nerve endings and could be just as effective as directly stimulating the vagus nerve. The latter requires surgically implanted electrodes.

In one study, led by Tracey's colleagues at the Feinstein Institute and GE Research, rats receiving a few minutes of ultrasound treatment to the spleen nerve had a diminished inflammatory response to an injected toxin. In another study, researchers at the University of Minnesota and their colleagues reduced symptoms of inflammatory arthritis in mice by stimulating their spleen nerves for 20 minutes every day for a week. Zeroing in on the spleen may provide a more precise approach than focusing on the vagus nerve, says Hubert Lim, lead author of the latter study. "When we're targeting the spleen, we have less of an effect all over the body."

Little is known about how repeated ultrasound affects the spleen or whether it has other harmful effects, says neuroscientist Denise Bellinger of Loma Linda University, who was not involved in either study. An ongoing clinical trial aims to assess the treatment's safety in humans with rheumatoid arthritis. A bigger unknown is how ultrasound activates nerves in general. Scientists are now exploring the use of ultrasound on other parts of the nervous system, including the brain. "We know how to control nerves with electricity, and we've been doing it for more than 100 years," Tracey says. "But the idea of controlling nerve signals with ultrasound is a brand-new field."

—Bahar Gholipour

DON JOHNSTON Getty Images

ECOLOGY

Deer Friends

Bats and white-tailed deer have each other's backs

Forget bug repellent—some deer in Minnesota rely on a team of bats to eat up the swarms of biting flies that typically plague them. Researchers observed this previously unknown symbiotic relationship between white-tailed deer and an unidentified bat species, in camera-trap footage and in person, at the Cedar Creek Ecosystem Science Reserve.

"These bats appear to be attracted by all the flies around the deer," says study leader Meredith Palmer, then a postdoctoral researcher at the University of Minnesota. Symbiotic relationships between grazing mammals and birds are better known, she says, but "it's very, very rare for mammals to engage with each other like this."

Horseflies and deerflies deliver painful bites that can fester and transmit disease, and the bats bring the deer much needed relief in the summer months. Meanwhile the deer act as lures, providing the bats with an all-you-can-eat fly buffet. "It decreases the search time" for bats to find food, Palmer says. "They aren't flying through an entire forest looking for flies." The study was published in March in *Ethology*.

Craig Willis, a biology professor at the University of Winnipeg in Manitoba, who was not involved in Palmer's research, says the findings hint at the pest-deterrent services bats may offer humans. "If the bats are reducing biting insects for deer, maybe they can also do the same for us," he says.

Ecological research often focuses on predator-prey interactions rather than on the positive ways in which animals help one another, Palmer notes. When it comes to mutually beneficial symbiotic relationships, she says, "there's just a big gap out there."

—Joshua Rapp Learn

ANIMAL COGNITION

Cats Know Their Names

Felines distinguish between their monikers and similar-sounding words

Cats are notorious for their indifference to humans: almost any owner will testify to how readily these animals ignore us when we call them. But a new study indicates domestic cats *do* recognize their own names—even if they walk away when they hear them.

Atsuko Saito, a behavioral scientist now at Sophia University in Tokyo, previously showed that cats can recognize their owner's voice. In her latest study, which involved 78 cats from Japanese households and a "cat café," she homed in on responses to their names.

Saito and her colleagues first had owners repeatedly say four words that sounded similar to their cats' names until the animals habituated to those words and stopped responding. Next the owners said the actual names, and the researchers looked at whether individual cats (when living among other cats) appeared able to distinguish their monikers. The cats had more pronounced responses to their own names—meowing or moving their ears, heads or tails—than to similar words or other cats' names, according to the study, which was published in April in *Scientific Reports*.

The researchers also had people unfamiliar to the cats speak the names. Although the felines' responses were less prominent than when their owners called them, they still appeared to recognize their names.

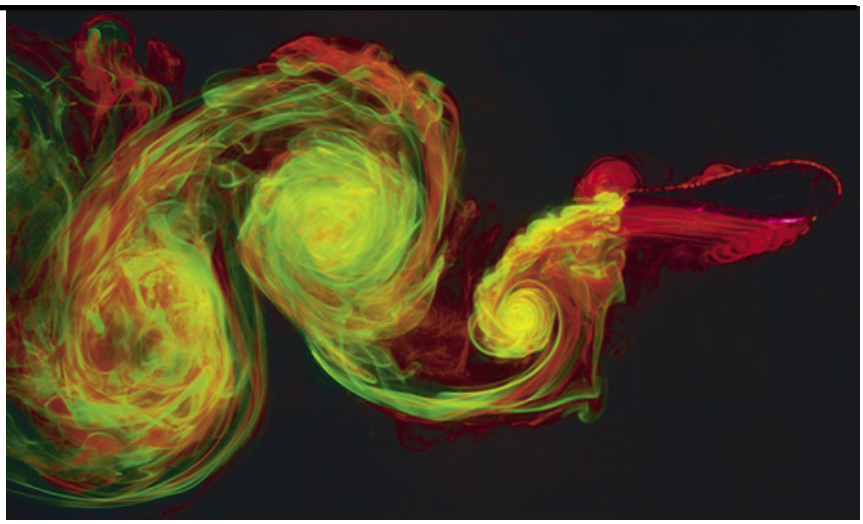
"This new study clearly shows that many cats react to their own names when spoken by their owners," says biologist John Bradshaw, who formerly studied human-animal interactions at the University of Bristol's Anthrozoology Institute and was not involved in the work. But Bradshaw says he is less convinced cats can recognize their names when spoken by someone unfamiliar. "I think that it's entirely possible that some cats are able to generalize between one human voice and another, but I'd like to see more trials before I'd say that the evidence is compelling," he says.

Saito says the felines in the experiments probably "associated their names with some rewards or punishments," and she thinks it is unlikely they understand that these sounds are attached to them as individuals. "There is no evidence that cats have the ability to recognize themselves, like us," she explains. "So the recognition [of] their name is different from ours." Still, it may be possible to teach cats to recognize other words. Whether that could allow humans to train cats to respond to commands—as dogs readily do—is another matter.

"Cats are just as good as dogs at learning," Bradshaw says. "They're just not as keen to show their owners what they've learned." —*Jim Daley*

"Cats are just as good as dogs at learning."
—John Bradshaw
University of Bristol

GETTY IMAGES



Nonideal wing shape generates vortices (*visualized here with red dye*) at its leading edge that interfere with trailing-edge vortices (*green dye*).

LEIF RISTROPH *Applied Mathematics Laboratory, Courant Institute of Mathematical Sciences, New York University*

BIOMECHANICS

Flight Simulator

Finding the ideal wing shape through evolution

Humans have long drawn inspiration from bird wings to design mechanical ones—and now a team of mathematicians has taken this biomimicry to a new level. By 3-D-printing a variety of wing shapes, racing them in a laboratory and feeding the data into an algorithm that simulates evolution, the researchers found that a teardrop-shaped wing is fastest for both flapping flight and swimming.

This is the first time such a combined process has been used to find an optimal wing shape for fast flight, says Leif Ristroph, a mathematician at New York University's Courant Institute of Mathematical Sciences and senior author of the new study.

Specific aspects of the teardrop shape help to make the optimal wing faster than its competitors, Ristroph says. These include its front-to-back asymmetry (when viewed from the side), characterized by a rounded front, forward placement of its thickest point and a slender, trailing tail. The razor-thin back edge resembles that of a bird wing, which typically narrows to a single feather. The finding suggests birds' wings have evolved to be as thin as possible, the researchers write in the study, which was published in January in the *Proceedings of the Royal Society A*.

Ristroph and his collaborators 3-D-printed a first "generation" of 10 plastic wings. They attached each wing to a motor-driven horizontal rod that caused it to flap up and down in water. They measured its swimming speed and extrapolated its flying speed. They tested a variety of shapes, including ones based on conventional airplane wings, flattened spheres and a peanutlike structure, Ristroph says.

The researchers fed the wing speed data into the evolutionary algorithm, which produced a second generation of eight "daughter" wings. Faster wing shapes were more likely to be passed on to the next generation, but the algorithm also allowed "mutations" that could yield new shapes. The two fastest wings from the first generation were also added to the second. The process of 3-D printing and laboratory racing was then repeated with the second generation of 10 wings. Altogether the researchers created 15 generations of wings. The fastest wing—the teardrop shape—evolved in the 11th generation and persisted in the following ones. The algorithm's attempts to improve this shape in subsequent generations yielded ones that were too slender to 3-D-print.

The study "is tremendously interesting," says Geoffrey Spedding, an aerospace engineer at the University of Southern California, who was not involved with the work. He notes that the optimal wing is "more like a fish fin," which makes it better suited for swimming or propelling objects forward than for generating lift, as in airplane flight. —*Rachel Crowell*

ANIMAL BEHAVIOR

Monkey Alarms

Some prey species send warning calls to scare off predators

Anthropologist Dara Adams was following a troop of six saki monkeys in Peru's Amazon rain forest, when out of nowhere they began shrieking, hooting and barking loudly. Suddenly, sleek and black as night, a small wildcat called a jaguarundi descended the trunk of a Brazil nut tree, leaped to the forest floor and ran off into the jungle.

Many animals use alarm calls to warn others in their species about a predator. But that does not entirely explain what Adams saw—because the monkeys continued calling even after the entire group became aware of the threat. A more tantalizing possibility is that the monkeys were addressing the cat itself, blowing its cover and warning it to call off the hunt.

This idea, which scientists call the "pursuit deterrence hypothesis," has been proposed in studies of birds, fish and mammals. But the vast majority of studies focus on the calling prey animal, rather than the impacts of those calls on the predators, Adams says. So she and her team from the Ohio State University decided to radio-collar two ocelots, another type of petite cat found in the Peruvian Amazon. While tracking the cats' movements, Adams and her colleagues used an unobtrusive loudspeaker to broadcast recorded alarm calls from titi and saki monkeys, two species ocelots prey on. They also played other types of social calls made by the monkeys.

The alarm calls proved an effective deterrent, prompting the ocelots to move away from the loudspeaker. When the cats heard the other types of calls, they either stayed still or moved in some random direction—but never as far away as when they heard the alarm ones, the team reported last November in *Animal Behaviour*. "Our study provides the first experimental evidence to show that wild ambush predators in natural conditions are deterred by prey alarm calls," Adams says.

Dan Blumstein, a biologist at the University of California, Los Angeles, who was not involved in the study, agrees that the findings suggest these monkeys' calls serve to warn off the cats. But he wonders, "Are they moving away out of fear of getting attacked by the monkeys? Or are they moving away because they know the game is up?" —*Jason G. Goldman*

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2

Toppin's titi monkey (*Callicebus toppini*) (*1*) and ocelot (*Leopardus pardalis*) (*2*).

JASON G. GOLDMAN (*1*); HAL BERAL *Getty Images* (*2*)

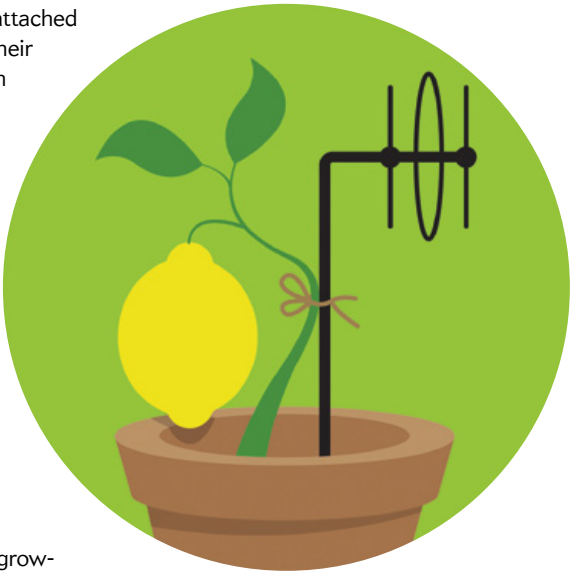
ENVIRONMENTAL TECH

The Internet of Plants

Scientists turn lemons into tiny "radio stations" that signal when a tree needs watering

Plants do not listen to the radio. But a team of researchers in Greece recently found a way to turn lemons into miniature "radio stations" that can broadcast information about their trees' moisture content to a smartphone—the first step toward creating what the researchers call an "Internet of plants."

Scientists had previously attached sensors to trees to measure their water use, but "no other team had created a wireless [radio] network among plants, transmitting information while consuming only a few microwatts and costing just a few dollars," says project leader Aggelos Bletsas, a professor of electrical and computer engineering at the Technical University of Crete.



The network consists of several basic components: an existing FM radio station, an antenna attached to a lemon growing on a tree, a humidity sensor in the lemon, a transistor connected to an antenna and an FM receiver (such as the kind found on a smartphone). First, the antenna picks up the ambient signal from the FM station. The antenna then passes the signal to the transistor, which is modulated by the humidity sensor. The sensor switches the transistor on and off at a rate dependent on the plant's moisture level: if the soil is wet or if the atmosphere is humid, that rate is lower; if it is dry, the rate is higher. Finally, the antenna broadcasts this information to the radio receiver on a mobile phone.

In this way, plants can tell farmers if they are thirsty. "We can literally 'listen' to the moisture of the plant, using our mobile FM radio with a €3 [$3.40] sensor," Bletsas says. "Two of these sensors for every acre on any given farm might change the way we [conduct] agriculture and 'understand' plants." He notes that more sensors may be needed for optimal results, particularly if the field slopes and cannot be watered evenly. Such real-time information could enable better control of air and soil moisture and possibly reduce the use of pesticides and optimize fertilization, the researchers say.

Why go through all this trouble and not just use already common wireless technology, such as Bluetooth? "Not only is our technique less complex, as we are just borrowing ambient signals in the environment," Bletsas says, but "a Bluetooth-based sensor costs about €22 [$25]. Our ultimate aim is to launch sensors onto the market costing less than $1."

Others have praised the idea. "Bletsas and his team are revolutionizing environmental sensing using very simple hardware and surprisingly little power," says Alexandros Dimakis, an associate professor of electrical and computer engineering at the University of Texas at Austin, who was not involved in the research. "Their work could be a transformational Internet of Things technology for agriculture and for monitoring the environment."

Bletsas and his colleagues have already applied for a patent for their innovative technology in the U.S.

—Stav Dimitropoulos

Illustration by Thomas Fuchs

Is Pot Any Good for Pain?

The data are spotty, but there's still a reasonable case to be made

By Claudia Wallis

"Medical cannabis saved my life," says Nancy Partyka, a retired college psychology instructor in Frisco, Colo. For more than 20 years Partyka battled agonizing pain stemming from a car crash that injured her cervical spine. She tried physical therapy, steroid injections, acupuncture, exercise and meditation. She endured five spinal fusion surgeries and plenty of pills. "I was taking OxyContin, taking Aleve by the handful," she recalls, but she was spiraling downward. "The narcotics suppress your appetite. You don't eat right, you are constipated, you feel worse. The dominos keep falling." Ultimately Partyka says she found relief in cannabis, which is legal in Colorado. Her preferred formula, taken in an edible form, combines the plant's two main active chemicals in a ratio of eight parts cannabidiol (CBD) to one part tetrahydrocannabinol (THC). She also uses a topical spray that is equal parts CBD and THC. "I have a life again," says Partyka, who is back to hiking and snowshoeing. "I'm not saying I'm 100 percent pain-free. But I'm off the opioids. I almost feel normal."

Anecdotes such as Partyka's are not hard to find. With opioids out of favor, and medical marijuana now legal in 33 states , many people with chronic pain are looking to the nation's budtenders for relief. Surveys suggest that pain is the single biggest reason Americans use medical marijuana, and although cannabis laws vary, all 33 states permit its use as an analgesic.

The validity of that choice got a big boost in 2017, when the National Academies of Sciences, Engineering, and Medicine released a detailed report concluding that there was "substantial evidence that cannabis is an effective treatment for chronic pain in adults." Still, the research leaves a lot to be desired. "The data are highly conflicting," says Sean Mackey, chief of the division of pain medicine at Stanford University Medical Center. He notes that a number of mostly small randomized clinical trials have shown "some benefit" for certain types of pain, but larger epidemiological studies are more equivocal or even negative.

A comprehensive review of the research published last year in the journal *Pain* breaks this down. It found that the strongest support for cannabinoids comes from studies of pain associated with multiple sclerosis and with nerve damage. "When it comes to the most common pain problems—back and neck pain, arthritis—very few studies have been done," says Gabrielle Campbell, a research fellow at the University of New South Wales in Australia and a coauthor of the review. "For arthritis, there was only one poor-quality study." Research quality was a problem overall, Campbell points out: just 15 studies out of 104 that were examined were highly rated for methodology, and only 21 had 100 or more participants.

Research has been inhibited by marijuana's status as a tightly regulated Schedule I drug. Scientists must have a special license to obtain it. Another challenge is the multiple forms of cannabis: endless smokable varieties, plant extracts that can be used topically or orally, edible gummies, and so on. In addition, the products people report using are not necessarily what they think they are. CBD oil may contain more or less CBD than advertised and include unlabeled THC. A 2017 study that examined 84 cannabidiol products bought online found that 69 percent misrepresented the content.

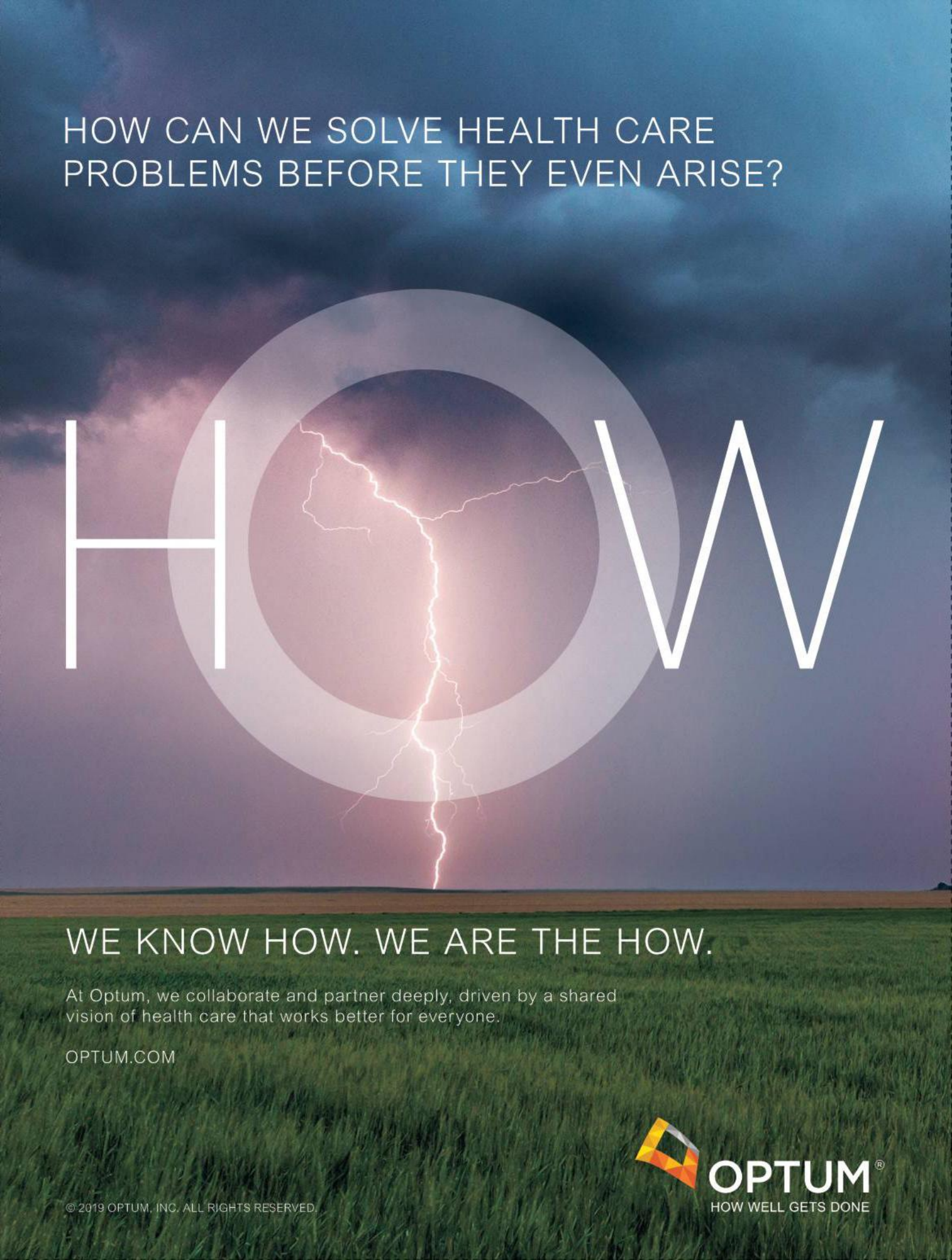
Much of the best research on cannabis and pain involves a pharmaceutical-grade product called nabiximols (Sativex), a plant extract approved in more than 25 countries for relief of muscle spasms and related pain due to multiple sclerosis. In the U.S., however, the only approved cannabinoids are synthetic drugs for treating nausea in cancer patients and a new plant-derived drug, Epidiolex , for rare forms of epilepsy. Nothing explicitly for pain.

It would be easy to conclude, as medical experts and health columnists so often do, that patients should simply wait for better data and better products. But chronic pain is an urgent problem for millions of people, many of whom, like Partyka, are not helped by standard therapies. "When you have a patient in front of you who has tried 14 different treatments, and you have multiple randomized controlled trials showing an effect for cannabis for that condition, then I think it's reasonable to try it if the patient is otherwise appropriate," says Kevin Hill, director of addiction psychiatry at Beth Israel Deaconess Medical Center in Boston.

Hill agrees with European and Canadian guidelines that view cannabis as a third-tier treatment for pain. As for the holes in the data, he has an interesting suggestion: In states where cannabis is legal and taxed, why not direct some of the revenues and a portion of the booming industry profits to finding answers? SA

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*.

Illustration by Celia Krampien



Safe Words for Our AI Friends

Virtual assistants are getting smarter. Let's think about how that will play out

By Wade Roush

In their latest iteration, Apple's popular AirPods wireless earbuds let you activate Siri, Apple's AI assistant, simply by saying, "Hey, Siri," just as you can with your iPhone. With the original AirPods, a physical tap on one AirPod would bring up Siri, but the voice command is simpler. And it takes us one step closer to a world where we can talk to our AIs and they to us anywhere, anytime.

It's a technology we've been anticipating for decades. From the *Enterprise* computer on the original *Star Trek* (1966–1969) to HAL 9000 in *2001: A Space Odyssey* (1968) to Samantha in Spike Jonze's *Her* (2013), science fiction has shown us all manner of disembodied AI helpmates who can answer our questions, carry out our orders or even provide emotional intimacy.

With the emergence of AIs like Siri, Google Assistant, Amazon's Alexa and Microsoft's Cortana, the idea is now a lot less fictional. I'd genuinely miss Alexa if I couldn't ask her to supply weather forecasts, keep my shopping list, control the lights in my house, and play podcasts and radio.

But AI assistants aren't yet omnipresent, and they aren't all that smart. Their arrival in our ear canals, plus some stunning recent progress in AI research, will change all that. In Silicon Valley, Google and OpenAI, a nonprofit research company, have been racing to apply advances in an area called unsupervised learning. Their latest language models cull existing texts on the Web to generate coherent, humanlike responses in question-answering and text-completion tasks. Within a couple of years these models will make AI assistants dramatically more capable and talkative.

Wade Roush is the host and producer of Soonish, a podcast about technology, culture, curiosity and the future. He is a co-founder of the podcast collective Hub & Spoke and a freelance reporter for print, online and radio outlets, such as *MIT Technology Review*, Xconomy, WBUR and WHYY.

And that means it's time to ask whether we *really* want AIs whispering in our ears all day—and if so, what conditions and controls we'd like to see implemented alongside them.

In last month's Ventures column, I looked at the ways Facebook's seemingly benign plan to connect people with one another went off the rails, resulting in a system of mass surveillance and manipulation. The same thing could happen with AI assistants if we don't insist on basic protections in advance. Let me suggest a few:

Privacy. Inevitably the smarts of our AIs will reside in the cloud, on servers owned by tech giants such as Amazon, Apple, Google and Microsoft. So our interactions with AIs should be encrypted end to end—unreadable even by the companies—and the records should be automatically deleted after a short period.

Transparency. AI providers must be up front about how they are handling our data, how customer behavior feeds back into improvements in the system, and how they are making money, without burying the details in unreadable, 50-page end-user license agreements.

Security and reliability. We will engage with our AI assistants in our homes, vehicles and workplaces across numerous Wi-Fi and (soon) 5G networks. We will be relying on them for advice, suggestions and answers, at the same time we will be giving them real-world tasks such as monitoring the performance of our appliances and the safety of our homes. We will need high availability, and every link in the communications chain must be hackerproof.

Trustworthiness. The same unsupervised learning algorithms that generate coherent conversation could be coopted to generate fake or misleading content—which is part of the reason OpenAI is not yet releasing its powerful new language models to the outside world. When we ask our AIs for answers, we'll need assurances that they are drawing on accurate data from trusted sources.

Autonomy. AI assistants should exist to give us more agency over our lives, not less. It would be a disaster for everyone if they morphed into vehicles for selling us things, stealing our attention or stoking our anxieties.

If the giant AI providers are allowed to self-regulate in these areas, the result will surely be more Facebook-style fiascoes. The push for protections will have to come from us, the users, and our representatives in government. After all, no one wants "Hey, Siri," to turn into "Bye, Siri." SA

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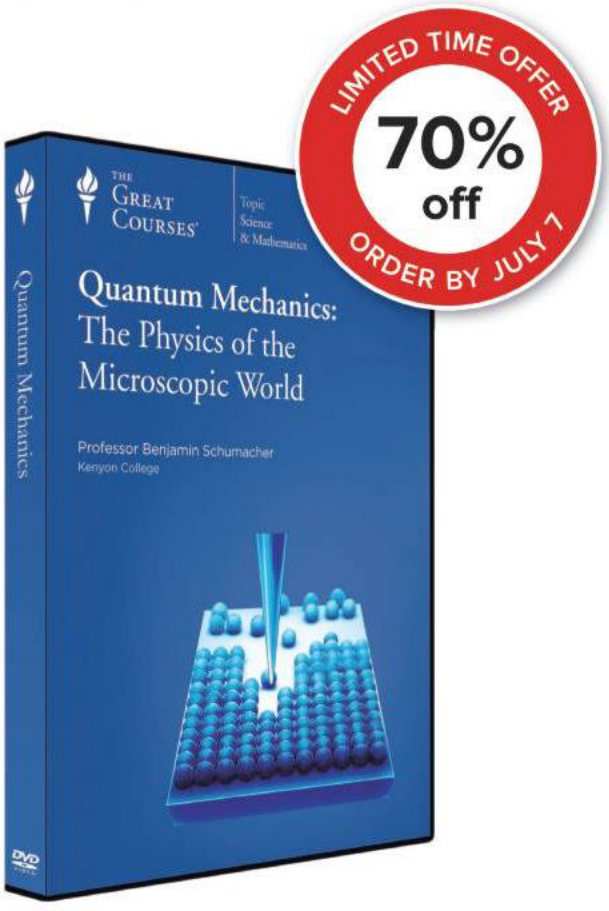

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The rise of Animals

New fossils and analyses of ancient ocean chemistry reveal the surprisingly deep roots of the Cambrian explosion

By Rachel A. Wood

Illustration by Franz Anthony

Rachel A. Wood is a paleontologist and geologist at the University of Edinburgh. Her research focuses on the origins and paleoecology of reefs and the evolution of seawater chemistry.

STAND ATOP THE STEEP WHITE CLIFFS THAT SURROUND THE giant rivers of Siberia, and your feet will mark a pivotal point in the history of life on Earth: the 541-million-year-old geologic boundary between the Precambrian and Cambrian periods. The rocks below this dividing line contain scant fossil remains—ghostly impressions of soft-bodied organisms and a smattering of shelly forms. But break open any of the rocks just above the boundary, and they will be teeming with shells. A little higher up still, familiar fossil creatures such as trilobites appear. These changes document the so-called Cambrian explosion, one of the most significant, but still poorly understood, events in all of evolution.

IN BRIEF

Scientists long thought that complex animals originated during the Cambrian explosion. **But mounting fossil** evidence indicates that they actually made their debut millions of years earlier, during the Ediacaran period. **New techniques** for reconstructing ancient ocean chemistry have yielded insights into the environmental pressures that drove this early evolutionary diversification.

For decades scientists thought that complex animals—multicellular organisms with differentiated tissue types—originated in the Cambrian explosion. To be sure, a riot of novel forms burst into existence during this time, including the ancestors of many of today's major animal groups. But recent discoveries from Siberia, Namibia and elsewhere show that complex animals actually got their start millions of years before the Cambrian explosion, during the last chapter of the Precambrian, known as the Ediacaran. Among these finds are the oldest known creatures with external and internal skeletons composed of mineralized tissue, a pivotal evolutionary innovation seen in many modern-day animals.

The presence of these armored creatures so far back in time—550 million years ago—indicates that the ecological and environmental pressures thought to have driven the Cambrian explosion were in fact at work long before then. Figuring out how these factors shaped the evolution of the earliest complex animals in the Ediacaran is key to understanding the astonishing burst of diversification that followed in the Cambrian.

The Cambrian fossil record has been the subject of intense study for more than 150 years. Thus, the broad global patterns of what Cambrian fossils appeared when—and where—are relatively well established: similar fossils turned up on many continents at around the same time, and they followed the same succession of evolutionary changes more or less synchronously. But only now, with the discoveries of the older Ediacaran fossils, are we starting to see the roots of the Cambrian explosion.

Gratifyingly, we are also beginning to puzzle out why it happened when it did, thanks in part to the development of new geochemical techniques that have revolutionized our understanding of the changing chemistry of the oceans in the Ediacaran-Cambrian world. Insights from the emerging fossil and geochemical records have just recently been integrated to show how the planet's biosphere, geosphere, hydrosphere and atmosphere—together known as the Earth system—may have operated during this interval. But already we can paint a striking picture of how the seafloor became successively populated by ever more complex creatures tens of millions of years before the Cambrian explosion, setting the stage for the rise of animal life as we know it.

THE FIRST ANIMALS

THE OLDEST POSSIBLE EVIDENCE of ancient animals comes not from recognizable fossils but from the remains of organic compounds known as biomarkers. Researchers have found one such biomarker, a particular form of sterane, in very well preserved rocks from a sedimentary sequence known as the Huqf Supergroup in Oman, which is at least 650 million years old. Some experts have argued that these steranes are unique to a particular group of sponges and that the presence of the molecules in the Huqf rocks therefore documents the existence of these animals at that very early time. Not all scientists accept the assertion that these steranes are specific to those sponges, however. Indeed, a study published in April suggests that they are diagnostic of a group of single-celled forms of amoebas.

The oldest candidate animal fossils, which hail from a sequence of rocks in southern China called the Lantian Formation and are possibly as old as 635 million years, are similarly contested. Some investigators think these tiny, soft-bodied forms are related to corals or jellyfish because they exhibit tentaclelike structures, but the preservation of these fossils is not sufficiently clear to allow unequivocal interpretation, leaving many researchers unconvinced that they represent animals of any kind.

The oldest animal remains that almost everyone can agree on are fossils from Newfoundland that date to about 571 million years ago, shortly after the last regional "Snowball Earth" glaciation that encased much of the planet in thick ice. These earliest known representatives of the Ediacaran biota were dominated by soft-bodied creatures up to a meter in height or width. Some took the form of large, featherlike fronds with vertical stalks that rooted them to the seafloor; others sprawled across the ocean bottom, their flat bodies exhibiting a fractal architecture, with branching units that showed the same patterns at all scales. All these body plans maximize surface area, suggesting that these animals absorbed nutrients directly from the surrounding water.

This modest variety of fauna prevailed for more than 10 million years. But then the pace of animal evolution began to accelerate. The fossil record indicates that after around 560 million years ago, the Ediacaran biota diversified to include mobile forms that inhabited shallow seas. Some of the fossils preserve scratch marks that suggest the animals were eating algal mats by grazing. Others may have dragged themselves across the algae, absorbing nutrients from the underside of their bodies. The first simple burrows also appear at around this time, evidence that animals had started to move and disturb the sediment of the seafloor.

Fast-forward to around 550 million years ago, and the oldest fossils preserving external and internal skeletons suddenly appear in limestone rocks (which consist mainly of calcium carbonate). These fossils are already diverse in size and form, and they show up in such far-flung locales as Siberia, Brazil and Namibia. The presence of skeletons in so many unrelated animal groups around the world at this point in time is testament to a major driving evolutionary force operating on a global scale. We do not know for sure what this force was. But we have an idea. Making a skeleton is energetically expensive, so for an animal to undertake such an endeavor the benefit must outweigh the cost. Animals may produce a skeleton for many reasons, but by far the most common is the need for protection from predators. Although there is no fossil evidence of predators from this time period, it stands to reason that the appearance of skeletons might reflect the first widespread occurrence of animals that ate other animals.

FOSSIL TRAIL: Key fossils of complex animals have come from Ediacaran rocks on the shores of the Yudoma River in Siberia (*1*) and on the edge of the Nama Desert in Namibia (*2*).

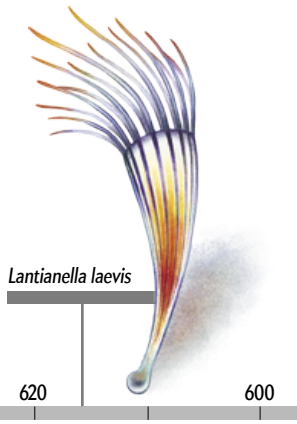
RACHEL A. WOOD

STRONGER TOGETHER

RECENT ANALYSES of these ancient skeletons have yielded tantalizing clues to what their owners looked like—and how they lived. Known from fossils of its delicate tubular skeleton that grew up to about 70 millimeters long and resembled a stack of ice cream cones, an organism called *Cloudina* has figured importantly in our reconstructions of Ediacaran ecosystems. *Cloudina* was first

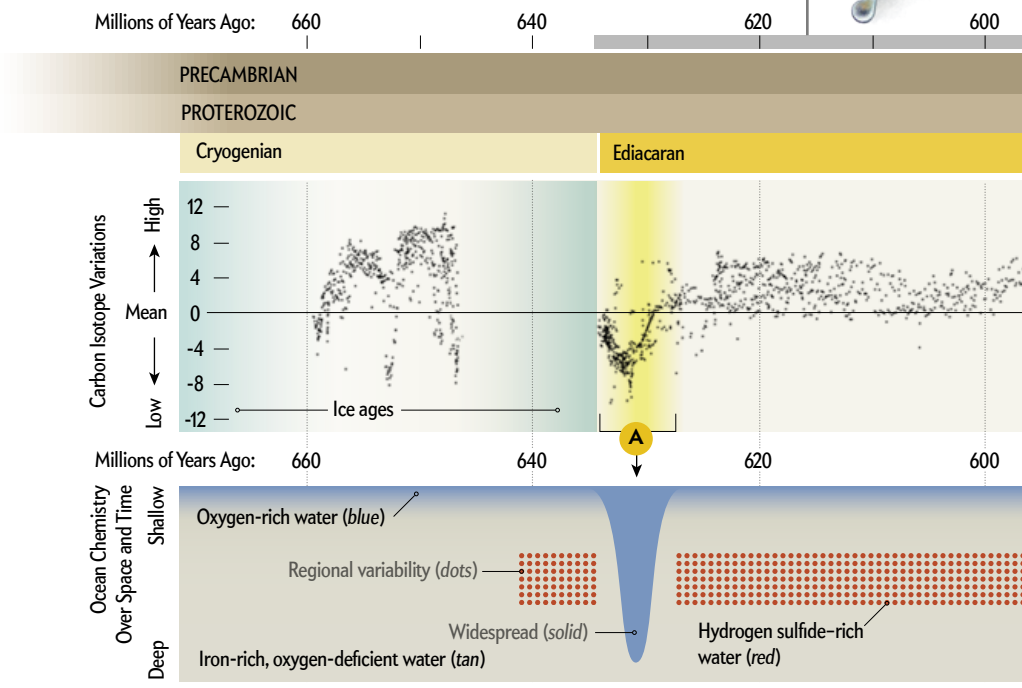
Before the Cambrian Explosion

Many key innovations in animal evolution that were traditionally thought to have originated in the Cambrian actually trace back much further in time to the Ediacaran. For example, the first animals with skeletons debuted during this earlier period. Their ability to produce mineralized tissue probably evolved as a means of protection from predators. Integrating the fossil and geochemical records spanning the time between 670 million and 480 million years ago reveals clues to the environmental factors driving this early evolutionary activity.



Geochemical Evidence

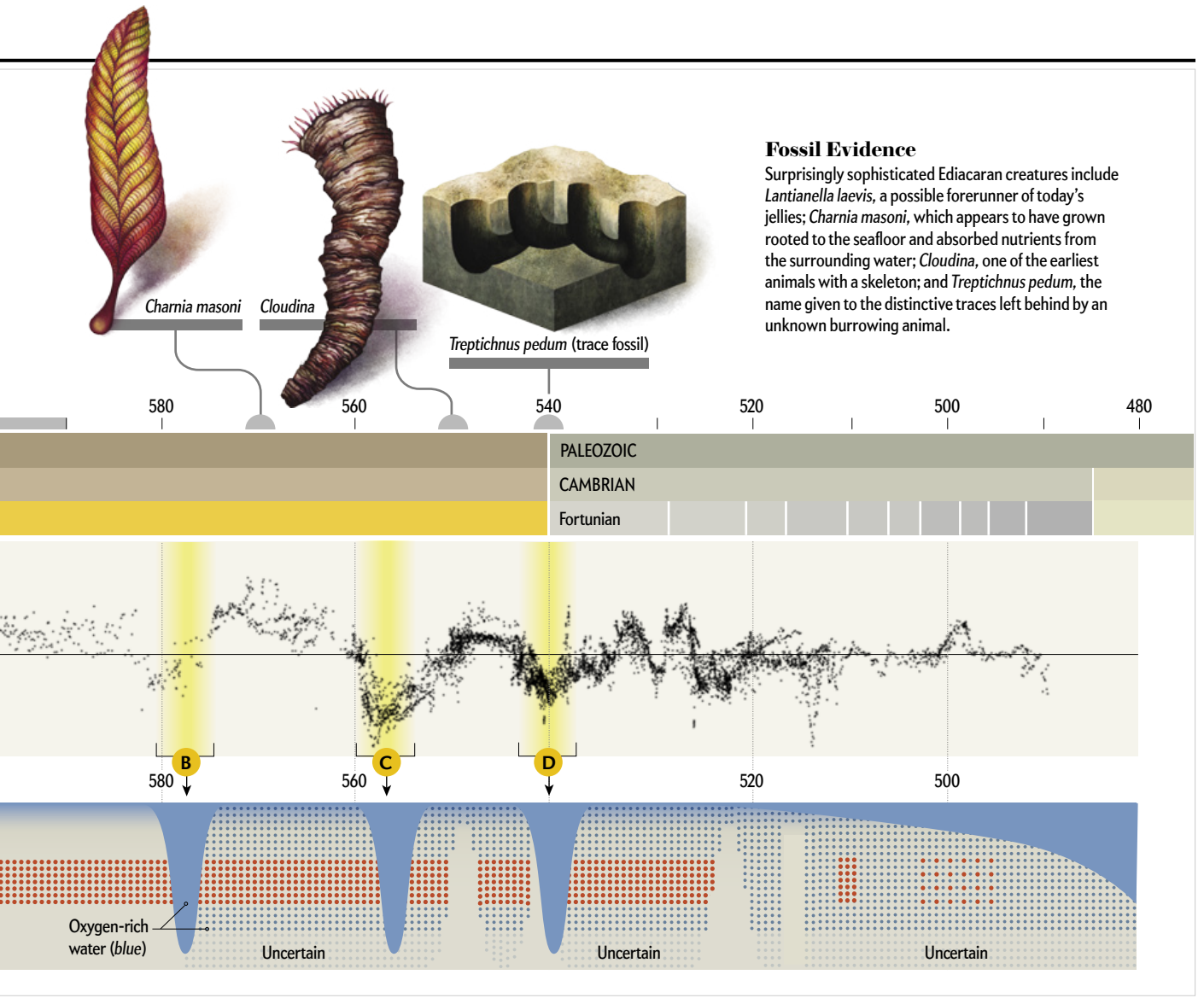
Animals need oxygen to survive. The evolutionary diversification that took place during the Ediacaran occurred under wildly fluctuating oxygen levels in the world's oceans. Carbon isotopes from Ediacaran rocks show that the carbon cycle was unstable and in a state of flux. Analyses of the iron compounds in these rocks, meanwhile, show that dissolved oxygen in the oceans probably reached a threshold or a series of thresholds in the Ediacaran that allowed animals to diversify by meeting their increased metabolic demands as they became more active. Researchers now believe the seas became progressively oxygenated not as one slow, gradual increase but in a series of episodes (A , B , C and D) that appear to coincide with the carbon isotope variations. This trend continued throughout the Ediacaran and probably well beyond.



discovered in Namibia in 1972 and was long assumed to have grown attached to the seafloor. But in the past few years researchers have identified many new specimens of *Cloudina* from sites around the world that have changed that view. My team's work on specimens from Namibia has shown that *Cloudina* had a variety of growth styles. It could attach to mats made of microbes that bound the soft sediment of the seafloor, or it could anchor itself to layered mounds of cyanobacteria. Most important of all, *Cloudina* individuals could actually cement themselves to one another to form a reef. This finding has established *Cloudina* as one of the oldest reef-building animals, pushing back the record of this way of life by some 20 million years.

Whether *Cloudina* was related to modern reef builders such as corals remains uncertain. But we do know that like reef-building corals, it lived in proximity to a number of other animals. Hints of this intimate association have come from other skeletal fossils found in rocks of the same age as those that contain *Cloudina* fossils. A creature called *Namacalathus,* known from fossil localities around the world, appears to have been one of *Cloudina*'s consorts. Its skeleton was up to 50 millimeters long, composed of a delicate, thin-walled stalk and a cup with a central opening at the top and several openings around the sides. The animal's soft tissue was probably mainly inside the cup, although it is never preserved. Fossils of *Namacalathus* indicate that it grew rooted to microbial mats, often near *Cloudina*.

Namapoikia, a creature known only from fossil localities in Namibia, also fraternized with *Cloudina*. This animal is remarkable for its large size—up to one meter in diameter—and robust skeleton. On the basis of its growth form, we think *Namapoikia* was a sponge and so would have had an internal skeleton, in contrast to the external skeletons *Cloudina* and *Namacalathus* probably had. Intriguingly, *Namapoikia* grew within the hidden places of reefs, encrusting the vertical walls of open cracks and fissures. In modern reefs



Fossil Evidence

Surprisingly sophisticated Ediacaran creatures include *Lantianella laevis*, a possible forerunner of today's jellies; *Charnia masoni*, which appears to have grown rooted to the seafloor and absorbed nutrients from the surrounding water; *Cloudina*, one of the earliest animals with a skeleton; and *Treptichnus pedum*, the name given to the distinctive traces left behind by an unknown burrowing animal.

SOURCE: "INTEGRATED RECORDS OF ENVIRONMENTAL CHANGE AND EVOLUTION CHALLENGE THE CAMBRIAN EXPLOSION," BY RACHEL WOOD ET AL., IN *NATURE ECOLOGY & EVOLUTION*, VOL. 3; APRIL 2019

the communities of animals and plants that live on open surfaces differ from those that occupy these more hidden areas such as caves, crevices or underhangs. Our Ediacaran fossil discoveries indicate that this distinction is as old as animal reefs themselves.

These observations are significant because reef building represents an important ecological innovation. By growing closely together and even cementing to one another, individuals can become mechanically stronger, rise above the seafloor away from competitors, enhance feeding efficiency and gain protection from predators. Like the earliest skeletons, then, the appearance of reefs in the Ediacaran fossil record may signal rising, complex ecological pressures. The Cambrian explosion, and indeed an arms race between predator and prey, had already begun.

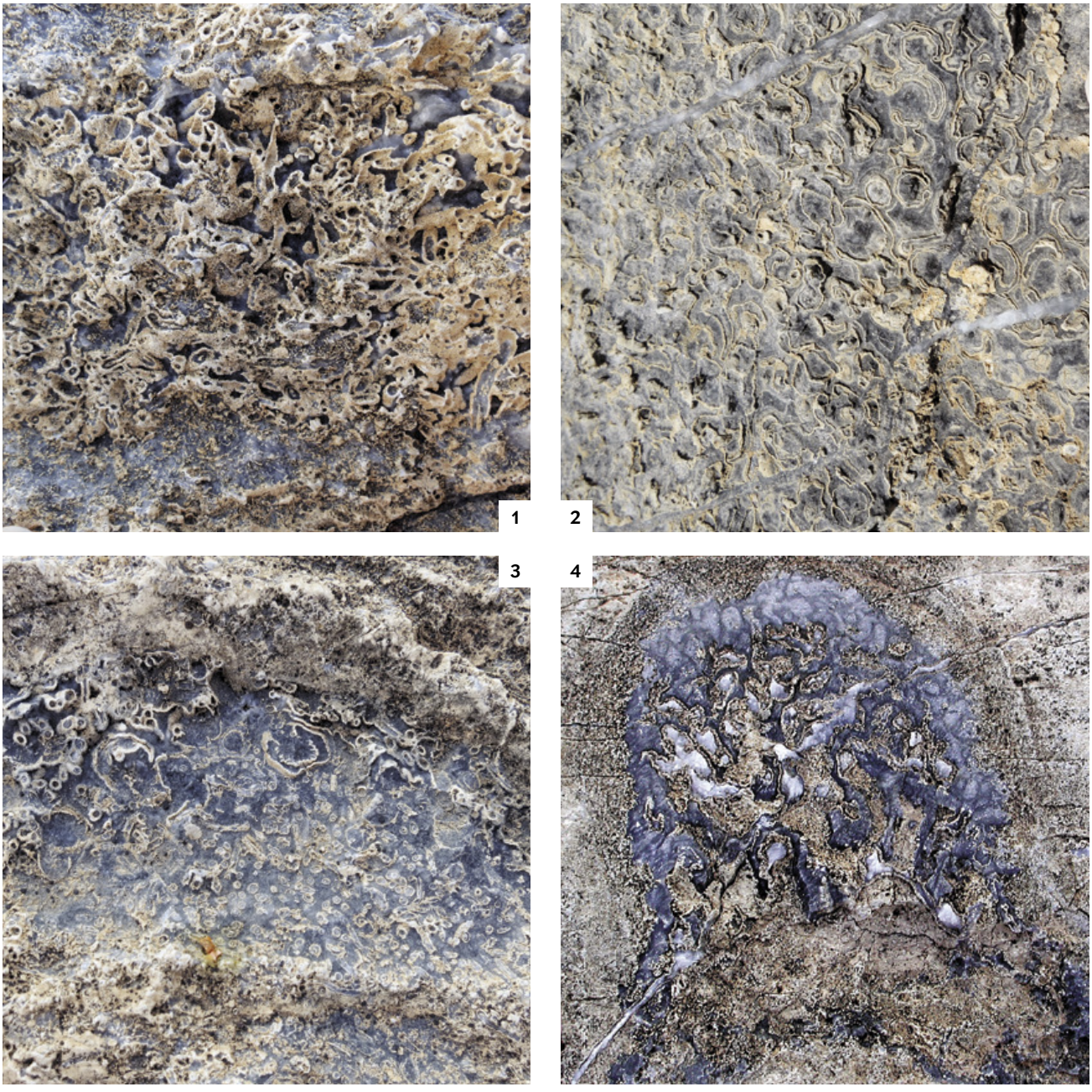
THE EDIACARAN WORLD

BY THE MID-2010S it was becoming clear that the Cambrian did not mark the sudden, dramatic departure from the Ediacaran that experts long envisioned. Not only had researchers begun to amass evidence that animals started evolving skeletons and building reefs earlier than traditionally thought, but we had also developed ecosystem models showing that Ediacaran animal communities shared many ecological traits with Cambrian ones. The "explosion," we were learning, had a far longer fuse than was previously recognized.

Then, a few years ago, some key discoveries in Siberia and China blurred the Ediacaran and Cambrian worlds even further. A group of researchers from China and Germany found that *Cloudina* persisted into the Cambrian. And my group, together with colleagues from Russia and China, found fossils long thought to be unique to the Cambrian in Ediacaran rocks. These findings underscored to us that to solve the mystery of the Cambrian explosion we had to figure out the dynamics of the Ediacaran world in which these animals originated.

The possible role of shifting oxygen availability is

Illustration by Franz Anthony (fossils)



WRITTEN IN STONE: *Cloudina* is one of the oldest organisms with an external skeleton, known from fossils that preserve its delicate, tubular armor (*1*). *Cloudina* individuals could cement themselves to one another, forming reefs. Another early skeletal form is *Namacalathus,* whose cup-shaped hard parts are typically preserved en masse (*2*). *Cloudina* and *Namacalathus* are often found together (*3*). *Namapoikia,* an early sponge, was another of *Cloudina*'s associates, one that grew in the hidden crevices of the reef (*4*).

one dynamic that researchers have been particularly keen to pin down. Animals need oxygen, so a central debate over the past few years has been to understand whether at some point in the time spanning the Ediacaran and Cambrian oxygen levels rose beyond a certain critical threshold, allowing animals to flourish. The question is more complicated than it might seem because animals do not all have the same oxygen requirements. Simple, immobile creatures, such as sponges, may need less oxygen than mobile animals, and they certainly require far less of the stuff than active, fast-swimming predators do. We have borne this variation in mind in the course of our investigations.

Fortunately for us, many new geochemical methods for estimating how much oxygen existed in these ancient seas have been developed in recent years. One especially powerful technique—Fe speciation—harnesses the characteristics of the various compounds of iron, which behave differently depending on whether oxygen is present or not. This method allows us to see

RACHEL A. WOOD

at a local scale where—and when—there was enough oxygen to support complex life. Studies carried out using this approach have led to a broad consensus: dissolved oxygen in the oceans probably reached a threshold or series of thresholds during the Ediacaran that allowed animals to diversify by meeting their increasing metabolic demands as they became more mobile and active.

Scientists have now assembled sufficiently large geochemical data sets that we can reconstruct how oxygen was distributed not just at individual Ediacaran sites of a certain age but globally through time. This work reveals patterns throughout the Ediacaran and early Cambrian that differ considerably from today's, with many areas showing a relatively thin veneer of well-oxygenated shallow waters laying atop a thicker wedge of deeper seawater that probably lacked oxygen altogether, a state known as anoxia.

These geochemical data also show that the boundary between the anoxic and oxic waters was very dynamic during this interval, rising and falling with shifting sea levels. Areas of shallow marine seafloor habitable to early animals were thus even more restricted than scientists expected—veritable oases of oxygenated water. If the evolutionary diversification that took place during the Ediacaran and Cambrian occurred under relatively low oxygen levels but with highly dynamic conditions that fluctuated on ecological, global and evolutionary timescales, how might these factors have shaped that extraordinary radiation?

ENGINE OF INNOVATION?

PERIODS OF INCREASED ANOXIA on the seafloor coincide with some well-known mass extinctions, such as the one that punctuated the Permian period 252 million years ago, killing off more than 90 percent of all marine species. But several major diversifications—including those in the Ediacaran-Cambrian, the Ordovician 100 million years later and the mid-late Triassic about 247 million years ago—began during long intervals of dynamic shallow marine anoxia. Considering these events, my colleague Doug Erwin of the Smithsonian Institution and I hypothesized that fluctuating oxygen conditions may have created critical opportunities for evolutionary innovation in soft-bodied animals.

It is far easier for animals to form a skeleton of limestone—the material that makes up the skeletons and shells of many modern marine creatures—when seawater oxygen levels exceed 10 micromoles per liter. Perhaps soft-bodied animals were only able to evolve these calcium carbonate skeletons once oxygen levels reached such a threshold, allowing formerly isolated oases to expand, connect and achieve stability on a global scale.

Much remains to be discovered about how life might have responded to changes in oxygen availability over evolutionary timescales. The response was probably complicated because animals were also contending with additional factors such as the rise of predation. And because feedbacks among individual organisms, ecosystems and the broader Earth system—which are largely unknown—would have also figured into the equation.

We have our work cut out for us. Dramatic changes in the regional processes that shaped Earth's crust throughout the Ediacaran-Cambrian interval have produced many significant gaps in the geologic and fossil record. This means that we have to piece together our narrative about the rise of complex animals from data collected from a multitude of localities all over the world. The fact that many of the key Ediacaran localities are still poorly dated further complicates our task. We typically date rocks of this age by measuring the ratio of lead to uranium in zircon crystals found in nearby layers of ash from ancient volcanic eruptions. This is one of the few methods that can supply an absolute, radiometric age for a given rock. But frustratingly, many of our best-known successions lack these vital ash beds. As a result, we are unable to accurately correlate evolutionary changes that have occurred in different parts of the world, which is essential for creating a solid timeframe for our history of events. A prime example is China's hotly debated Lantian Formation, which has yielded the oldest candidate animal fossils, but whose age could fall anywhere between 635 million and 590 million years.

Nevertheless, there are reasons for optimism. New ash beds are coming to light, and dating methods are being refined. For instance, the ash beds that many research groups use to calculate the ages of the Ediacaran fossils found in Namibia have recently been redated, and the youngest ones—those nearest the Precambrian-Cambrian boundary—have proved to be more than two million years younger than previously thought. This result raises important questions about how these fossils actually correlate with their counterparts in Newfoundland and Siberia, among other key localities. In addition, geochemists are developing new isotopic techniques and other methods that can bring our picture of oxygen conditions in this ancient world into sharper focus. And my team and others are finding new fossils in remote places that have gone largely unexplored until now, such as Siberia.

Sometime in the not so distant future, when we stand on those cliffs, surveying the vast forest below, we will have a far deeper understanding of this most extraordinary slice of time. SA

MORE TO EXPLORE

Low-Oxygen Waters Limited Habitable Space for Early Animals. R. Tostevin et al. in *Nature Communications,* Vol. 7, Article No. 12818; September 23, 2016.

A Deep Root for the Cambrian Explosion: Implications of New Bio- and Chemostratigraphy from the Siberian Platform. M. Zhu et al. in *Geology,* Vol. 45, No. 5, pages 459–462; May 1, 2017.

Integrated Records of Environmental Change and Evolution Challenge the Cambrian Explosion. Rachel Wood et al. in *Nature Ecology & Evolution,* Vol. 3, pages 528–538; April 2019.

FROM OUR ARCHIVES

The Big Bang of Animal Evolution. Jeffrey S. Levinton; November 1992.

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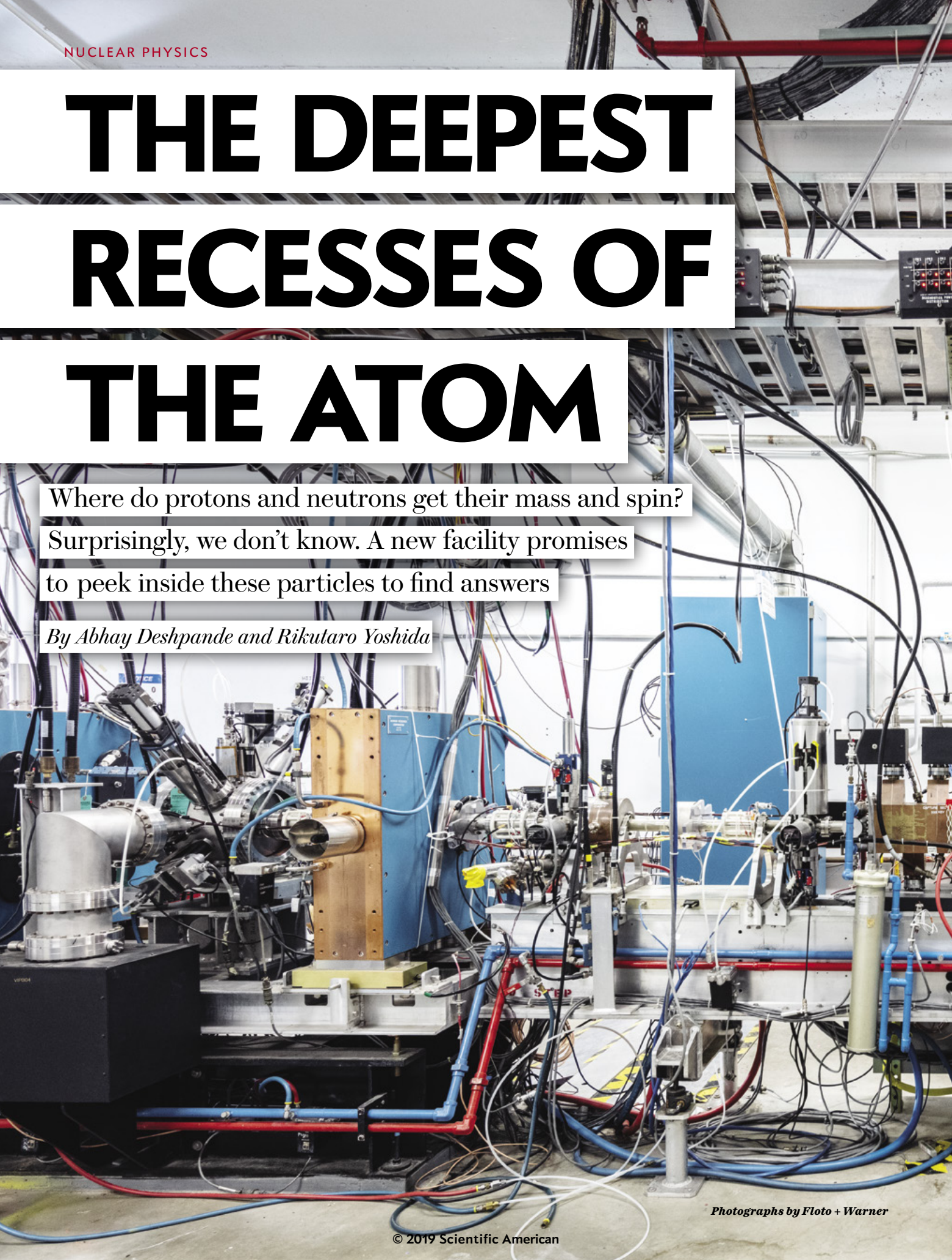
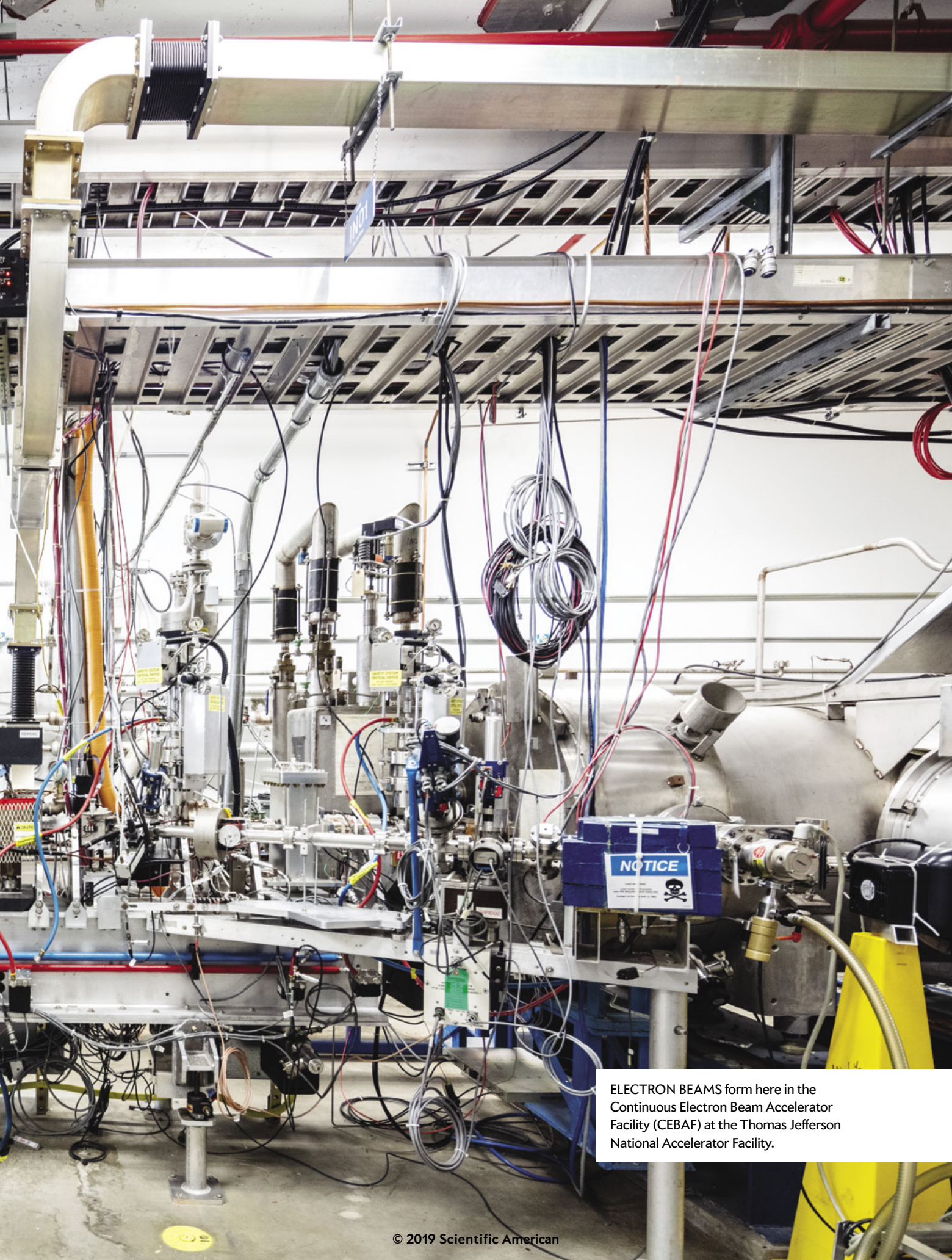
THE DEEPEST RECESSES OF THE ATOM

Where do protons and neutrons get their mass and spin? Surprisingly, we don't know. A new facility promises to peek inside these particles to find answers

By Abhay Deshpande and Rikutaro Yoshida



Photographs by Floto + Warner



ELECTRON BEAMS form here in the Continuous Electron Beam Accelerator Facility (CEBAF) at the Thomas Jefferson National Accelerator Facility.

Abhay Deshpande is a professor of physics at Stony Brook University and founding director of the Center for Frontiers in Nuclear Science, aimed at the scientific development and promotion of the Electron-Ion Collider (EIC).

Rikutaro Yoshida is a principal scientist at the Thomas Jefferson National Accelerator Facility. He is also the director of the EIC Center, which helps to advance and promote the science program of the future facility.

THE OBSERVABLE UNIVERSE IS ESTIMATED TO CONTAIN ABOUT 10^{53} KILOGRAMS of ordinary matter, most of that in the form of some 10^{80} protons and neutrons, which, along with electrons, are the ingredients of atoms. But what gives protons and neutrons their mass?

IN BRIEF

Where do protons and neutrons get their mass and spin? Surprisingly, scientists do not really know. **Somehow the ingredients** of these particles—quarks and gluons—combine in complex interactions that produce the properties of protons and neutrons. **To understand how,** physicists want to build an Electron-Ion Collider that would smash protons and atomic nuclei with electrons to provide 3-D pictures of nuclei interiors.

The answer, it turns out, is not simple. Protons and neutrons are made up of particles called quarks and binding particles known as gluons. Gluons are massless, and the sum of the masses of the quarks inside protons and neutrons (collectively "nucleons") makes up roughly 2 percent of the nucleons' total mass. So where does the rest come from?

That is not the only mystery of these basic atomic pieces. Nucleons' spin is similarly inexplicable—the spin of the quarks inside them cannot account for it. Scientists now think that spin, mass and other nucleon properties result from the complex interactions of the quarks and gluons within. But precisely how this happens is unknown. Theory can tell scientists only so much because the interactions of quarks and gluons are ruled by a theory called quantum chromodynamics (QCD), which is devilishly difficult to compute.

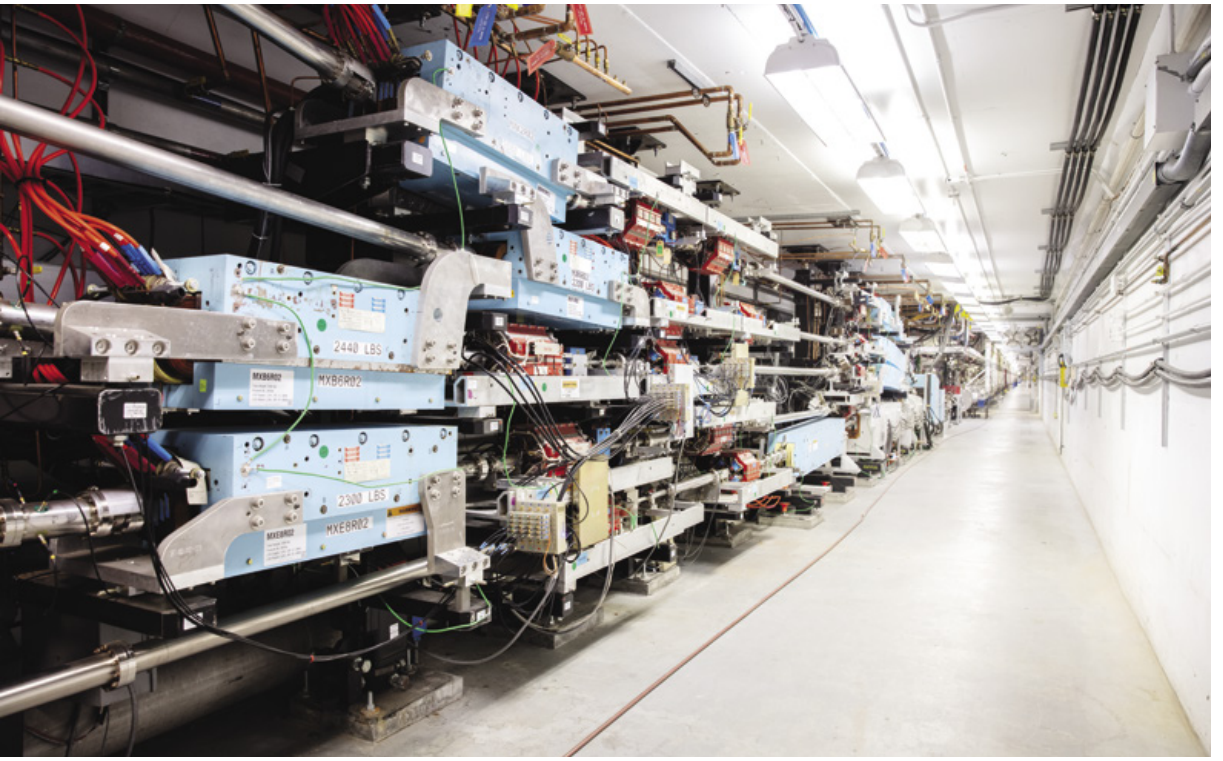
To move forward, we need new experimental data. That is where the Electron-Ion Collider (EIC) comes in. Unlike other atom smashers, such as CERN'S Large Hadron Collider near Geneva or the Relativistic Heavy Ion Collider (RHIC) in the U.S., which collide composite particles such as protons and ions, the EIC would collide protons and neutrons with electrons. The latter have no internal structure and become a kind of microscope to see inside the composite particles.

The EIC is one of the highest priorities of the U.S. nuclear science community and would most likely be built at one of two U.S. physics laboratories—Brookhaven National Laboratory on Long Island or the Thomas Jefferson National Accelerator Facility (Jefferson Lab) in Newport News, Va. If approved, the collider could begin collecting data around 2030. The machine will be able to see how the individual spin and mass of quarks and gluons, as well as the energy of their collective motion, combine to create the spin and mass of protons and neutrons. It should also answer other questions, such as whether quarks and gluons are clumped together or spread out inside nucleons, how fast they move and what role these interactions play in binding nucleons together in nuclei. The measurements at the EIC will deliver a trove of new information about how the basic constituents of matter interact with one another to form the visible universe. Fifty years after the discovery of the quark, we are finally at the threshold of unraveling its mysteries.

EMERGENT PHENOMENA

SCIENTISTS UNDERSTAND quite well how objects are made of atoms and how the characteristics of those objects arise from the characteristics of the atoms inside them. Indeed, much of our modern lives depends on our knowledge of atoms, electrons and electromagnetism—this knowledge is what makes our cars go and our smartphones work. So why is it that we do not understand how nucleons are made of quarks and gluons? First of all, nucleons are at least 10,000 times smaller than a proton, so there is no easy way to study them. Furthermore, the characteristics of the nucleons arise out of the collective behavior of quarks and gluons. They are, in fact, emergent phenomena, the outcome of many complex players whose interactions are too elaborate for us to fully understand at this point.

The theory that governs these interactions, quantum chromodynamics, was developed in the late 1960s and early 1970s. It is part of the overarching theory of parti-



BLUE DIPOLE MAGNETS help to steer electron beams as they accelerate around the CEBAF loop.

cle physics called the Standard Model, which describes the known forces of the universe (apart from gravity). Just as the electromagnetic force between electrically charged particles is carried by photons, or particles of light, QCD tells us that the strong force—the force holding nucleons together—is carried by gluons. The "charge" involved in the strong force is called "color" (hence "chromodynamics"). Quarks carry color charge and interact with one another by exchanging gluons. But unlike electromagnetism, where photons themselves have no electric charge, gluons carry color. Therefore, gluons interact with other gluons by exchanging more gluons. This wrinkle has profound implications. The feedback loop of interactions is why QCD is often too complicated to compute.

QCD also differs from more familiar theories because the strong force becomes weaker the closer together quarks get. (In electromagnetism, the opposite is true, and the force gets weaker as charged particles move farther apart.) At short enough distances within the nucleon, the quarks feel so little force they behave as if they are free. The discovery of this strange consequence of QCD won physicists David Gross, H. David Politzer and Frank Wilczek the 2004 Nobel Prize in Physics. When quarks move away from one another, the force between them grows rapidly and becomes so strong that quarks end up "confined" within the nucleon—that is why you will never find a quark or a gluon alone outside a proton or neutron. Scientists can calculate QCD interactions as long as the quarks are close together and interact weakly with one another; when they are farther apart, however—at distances close to the radius of the proton—the force becomes too strong, and the theory becomes too complex to be useful.

To understand the quantum realm of the strong force further, we need more information. Our mastery of the atomic realm, for example, did not come only from our understanding of atoms and their interactions—it came from our grasp of the emergent phenomena that arise on top of these fundamental building blocks. It was not possible to construct molecular biology from our knowledge of its foundations—atoms and electromagnetism. The eureka moment came when researchers discovered the double-helix structure of DNA. What we need to make progress in the quark-gluon world is to look inside the nucleus.

"SEEING" ATOMS

IN THE FIRST PART of the 20th century physicists discovered how to "see" atoms through a process called x-ray diffraction. By shining a beam of x-rays at a sample and studying the interference pattern that results when they pass through the material, scientists could see its atomic crystal structure. The reason this technology works is that the wavelength of an x-ray is similar to the size of an atom, giving us the ability to probe the atomic distance scale of nanometers (10^{-9} meter). In the same way, physicists first "saw" quarks 50 years ago in an experiment that collided electrons and protons in a process called deep inelastic scattering, or DIS.

In this method, an electron bounces off a proton (or neutron or nucleus) and exchanges a virtual photon with it. The virtual photon is not exactly real—it pops in and out of existence quickly as a consequence

Probing the Nucleus

Deep inelastic scattering (DIS) is a technique for studying atomic nuclei by hitting them with a beam of electrons at high speed. A new planned DIS facility called the Electron Ion Collider (EIC), proposed to be built at one of two U.S. laboratories (*right*), would provide 3-D pictures of the inside of protons, neutrons and atomic nuclei. With the EIC, scientists hope to solve the mystery of where protons and neutrons get their mass and spin—neither property can be accounted for by adding up the masses and spins of the quarks and gluons that make up these particles. Researchers also want to understand how the interactions between protons and neutrons arise from the quarks and gluons.

HOW DEEP INELASTIC SCATTERING WORKS

In DIS, an electron exchanges a "virtual photon"—a semi-real particle that pops into and out of existence quickly—with the quarks inside a proton or neutron. By analyzing the energy and recoiling angle of the electron as it bounces off, scientists learn about the object it hit. The higher the energy of the collision, the smaller the wavelength of the virtual photon, effectively creating a smaller probe that can "see" tinier scales within the nucleus.

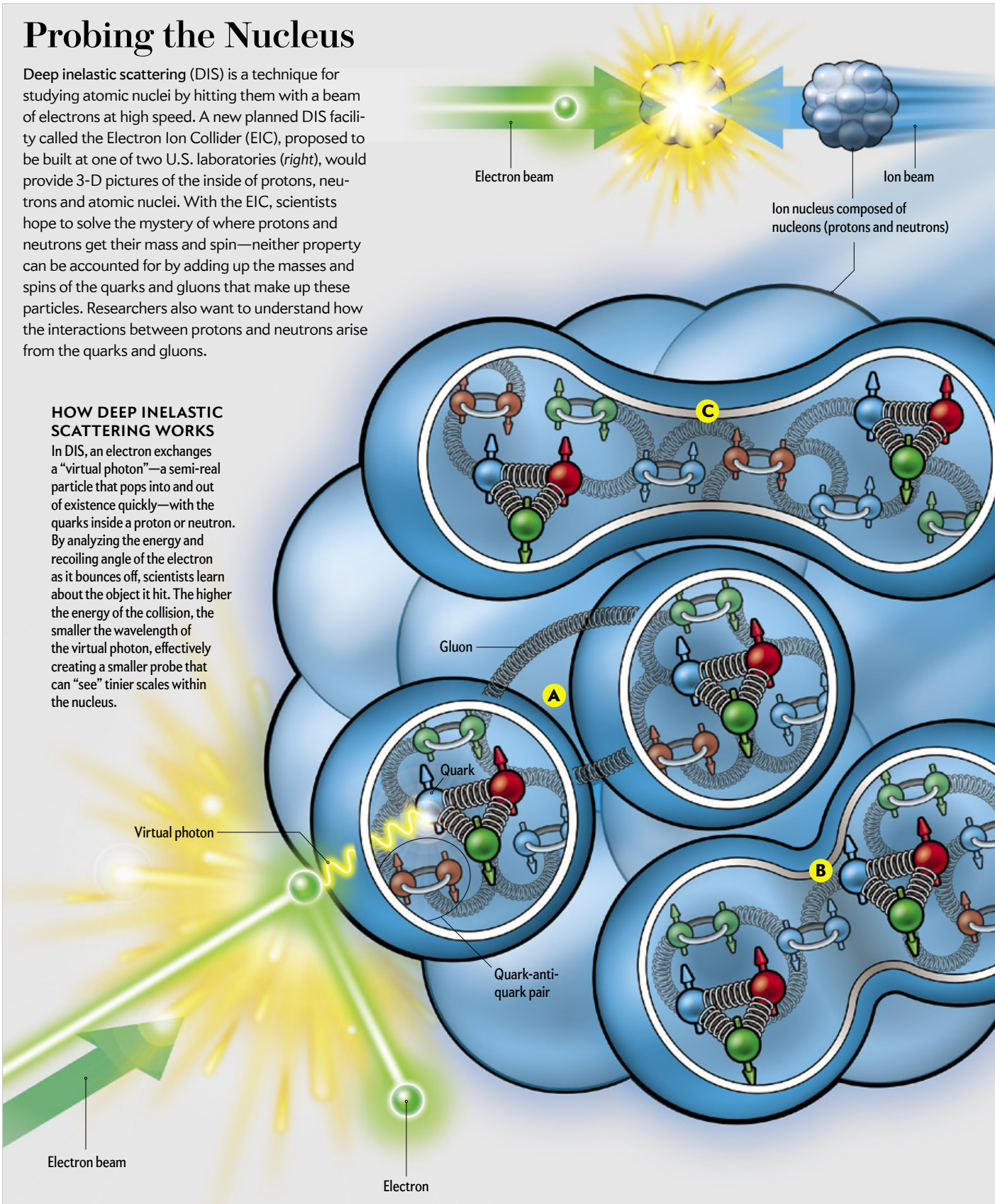
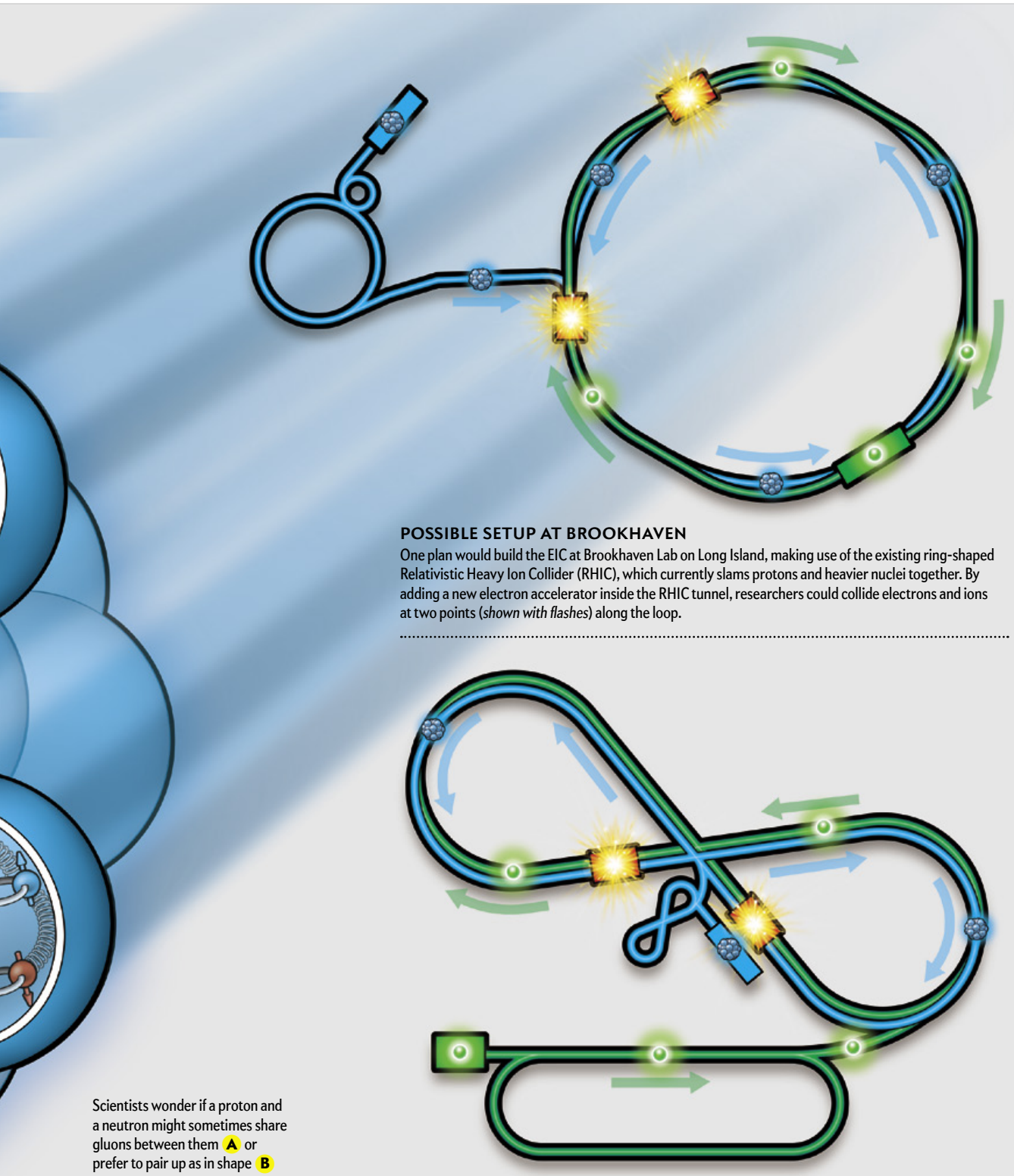


Illustration by Ben Gilliland



Scientists wonder if a proton and a neutron might sometimes share gluons between them **A** or prefer to pair up as in shape **B** or interact by exchanging quark-antiquark pairs **C**.

POSSIBLE SETUP AT BROOKHAVEN

One plan would build the EIC at Brookhaven Lab on Long Island, making use of the existing ring-shaped Relativistic Heavy Ion Collider (RHIC), which currently slams protons and heavier nuclei together. By adding a new electron accelerator inside the RHIC tunnel, researchers could collide electrons and ions at two points (*shown with flashes*) along the loop.

POSSIBLE SETUP AT JEFFERSON LAB

Another option would extend the recently upgraded electron accelerator called the Continuous Electron Beam Accelerator Facility (CEBAF, *bottom green loop*) at the Thomas Jefferson National Accelerator Facility in Newport News, Va. The electron beam would continue into a figure-eight-shaped "ring," and a new ion accelerator (*in blue*) running in the opposite direction would be added. Collisions between the two beams would occur at two points.

HEAVY IONS and polarized protons accelerate inside Brookhaven National Laboratory's Relativistic Heavy Ion Collider (RHIC).

of quantum mechanics, which governs particle interactions. By carefully measuring the energy and angle of the electron as it recoils, we gain information about what it hit.

The virtual photon's wavelength in DIS experiments is on the order of femtometers (10^{-15} meter)—the distance scale of the proton diameter. The higher the energy of the collision, the smaller the virtual photon's wavelength, and the smaller the wavelength, the more precise and localized the probe. If it is small enough, the electron in essence bounces off one of the quarks inside the proton (rather than the whole proton itself), providing a peek at the particle's inner structure.

The first DIS experiment was the SLAC-M.I.T. project at the facility then called the Stanford Linear Accelerator Center (SLAC). In 1968 it provided the first evidence of quarks—a discovery that won the experiment's leaders the 1990 Nobel Prize in Physics. Similar experiments discovered that quarks inside free protons and neutrons and those inside nuclei behave very differently. Furthermore, they found that proton and neutron spin does not come from the spins of the constituent quarks, as scientists had expected. This finding was first made in protons and initially called the "proton spin crisis." The first DIS collider, in which both electrons and protons were accelerated before crashing, was the Hadron-Electron Ring Accelerator (HERA) at the German Electron Synchrotron (DESY) research center in Hamburg, Germany, which ran from 1992 to 2007. The HERA experiments showed that what we thought was a simple configuration of three quarks inside each proton and neutron could in fact become a particle soup in which many quarks and gluons instantly appear and disappear. HERA significantly advanced our understanding of the structure of nucleons but could not address the Spin Crisis and lacked the beams of nuclei necessary to study quark and gluon behavior in the nuclei.

A major factor complicating all observations at this scale is the weirdness of quantum mechanics. These rules describe subatomic particles as hazes of probability: they do not exist in specific states at specific places and times. Instead we must think of quarks as existing in an infinite number of quantum configurations simultaneously. Furthermore, we must consider the quantum-mechanical phenomenon of entanglement, in which two particles can become connected so that their fates are intertwined even after they separate. Entanglement could pose a fundamental problem for observing at the nuclear scale because the quarks and gluons we would like to observe are at risk of becoming entangled with whatever probe we use to look at them—in the case of DIS, the virtual photon. It seems impossible to define what we mean by nucleon structure when what we find depends on how we probe it.

Luckily, by the 1970s QCD had advanced enough for scientists to figure out that the probe and the target in DIS experiments can be separated—a condition called factorization. At high-enough energies, scientists can essentially ignore the effects of quantum entanglement under certain circumstances—enough to describe the structure of the proton in one dimension. This meant that they could extract from DIS experiments a measurement of the probability that any given quark inside a proton is contributing a particular share of its forward momentum.

Recently theoretical advancements have enabled us to push further and describe the inner structure of nucleons in more than one dimension—not just how much quarks and gluons contribute to its forward momentum but how much they move side to side inside the nucleon as well.

But the real step forward will come with the EIC.

ELECTRON-ION COLLIDER

THE EIC WILL make a three-dimensional map of the interior of a nucleon. We expect the collider to deliver measurements of the positions and momenta of quarks and gluons and the amount each contributes to the nucleon's overall mass and spin.

The key advance of the EIC compared with previous DIS experiments is its brightness: it will produce between 100 and 1,000 more collisions per minute than HERA, for instance. In addition, the high energies of the colliding beams at the EIC will resolve distances of several hundredths the diameter of a proton, enabling us to investigate the regions where a large number of quarks and gluons each carry roughly 0.01 percent of the proton's forward momentum. The EIC will also let us control the alignment of the spin of the particles in its beams so that we can study how the spin of the proton arises from the QCD interactions of quarks and gluons. When incorporated into our modern theoretical framework, the EIC's measurements will allow us to create a truly 3-D image of the proton in terms of quarks and gluons.

BROOKHAVEN NATIONAL LABORATORY

We have many questions we hope to explore: For instance, are the constituents of the proton equally spread out within it, or do they clump together? Do some contribute more toward the particle's mass and spin than others? And what role do quarks and gluons play in binding together protons and neutrons to form nuclei? These quandaries are only beginning to be explored at existing facilities on the femtoscopic level. The EIC is the first machine that will lead us to complete answers.

One of the biggest unknowns in our conception of nucleon structure is what happens when we look at these particles with an extremely fine probe at very small scales. Here strange things start to happen. QCD predicts that as you probe at higher and higher energies, you will find more and more gluons. Quarks can radiate gluons, and those gluons in turn radiate more gluons, creating a chain reaction. Strangely, it is not the action of measurement that causes this gluon radiation but the weirdness of quantum mechanics that tells us the inside of the proton is different—there are simply more gluons—the closer you look.

Yet we know this cannot be the entire solution, because that would mean matter is growing with no limit—in other words, atoms would have an infinite number of gluons the closer you looked at them. Previous colliders, including HERA, have seen hints of a state of "saturation," in which the proton simply cannot fit any more gluons and some start to recombine, canceling out the growth. Physicists have never detected saturation unambiguously, and we do not know the threshold at which it occurs. Some calculations suggest that gluon saturation forms a novel state of matter: a "color glass condensate" with extraordinary properties. For instance, the energy density of gluons may reach an unprecedented 50 to 100 times the energy density inside neutron stars. To reach regions of the highest possible gluon density, the EIC will use heavy nuclei instead of protons to detect this fascinating phenomenon and study it in detail.

BUILDING THE EIC

PLANS FOR THE NEW COLLIDER have strong endorsements from the most recent (2015) long-range planning meeting of the U.S. nuclear science community as well as the U.S. Department of Energy, which in 2017 requested an independent evaluation of the EIC from the U.S. National Academies of Sciences, Engineering, and Medicine (NAS). In July 2018 the NAS committee found the scientific case for the EIC to be fundamental, compelling and timely.

There are two possible paths for building this machine. One would upgrade the RHIC at Brookhaven. This plan, dubbed the eRHIC, would add an electron beam inside the existing RHIC accelerator tunnel and have it collide at two different points with one of the RHIC's ion beams.

Another possibility is to use the electron beam at the Continuous Electron Beam Accelerator Facility (CEBAF) at Jefferson Lab. Under a design called the Jefferson Lab EIC (JLEIC), the CEBAF beam would be routed into a new collider tunnel to be built next door.

Either of these facilities would provide a huge leap in our understanding of QCD and, at last, a visualization of the interior of nucleons and nuclei. Either should allow us to tackle the questions of spin, mass and other characteristics of nucleons that have perplexed us so far. And either would have the capability to collide many species of nuclei, including heavy gold, lead and uranium, which would enable us to study how the spread of quarks and gluons changes when their nucleons are part of larger nuclei. We would like to know, for instance, whether some gluons begin to overlap and become "shared" by two different protons.

FEMTOTECHNOLOGY?

IN THE 21ST CENTURY the very size of the atom is the limiting factor in our technologies. In the absence of a major breakthrough, the length of 10 nanometers (about 100 atoms wide) is probably as small as electronic parts will get, suggesting that conventional computing power is unlikely to advance in the future at the rate it has for more than 50 years.

Yet nucleons and their internal structure exist at a scale a million times smaller. The strong force that governs this realm is roughly 100 times stronger than the electromagnetic force that powers current electronics—in fact, it is the strongest force in the universe. Might it be possible to create "femtotechnology" that works by manipulating quarks and gluons? By some measure, this kind of technology would be a million times more powerful than current nanotechnology. Of course, this dream is a speculation for the far-off future. But to get there, we first have to gain a deep understanding of the quantum world of quarks and gluons.

The EIC is the only experimental facility being considered in the world that could provide the data needed to understand QCD to the fullest extent. Building the EIC, however, will not be without its challenges. The project must deliver very bright and highly focused beams of electrons, protons and other atomic nuclei over a wide range in energies to create 100 to 1,000 times more events per minute than the HERA collider. The spin studies demand that the machine provide beams of particles whose spins are maximally aligned and can be controlled and manipulated. These challenges will require innovations that promise to transform accelerator science, not only for the benefit of nuclear physics but also for future accelerators studying medicine, materials science and elementary particle physics. SA

MORE TO EXPLORE

An Assessment of U.S.-Based Electron-Ion Collider Science. National Academies of Sciences, Engineering, and Medicine. National Academies Press, 2018. https://doi.org/10.17226/25171

FROM OUR ARCHIVES

The Glue That Binds Us. Rolf Ent, Thomas Ullrich and Raju Venugopalan; May 2015.

scientificamerican.com/magazine/sa

ETHOLOGY

ONE EYE OPEN

Why dolphins, seals and other animals developed the capacity to sleep with half their brain awake

By Gian Gastone Mascetti

Illustration by Giulia Neri

Gian Gastone Mascetti is a senior scholar of neurophysiology in the department of general psychology at the University of Padova in Italy, where he retired as a professor of neurophysiology. His research interests are focused on sleep, particularly the relation between sleep and brain lateralization.

ONE OF THE MOST STRIKING FEATURES OF LIVING ORGANISMS, both animals and plants, is the way their physiology and behavior have adapted to follow the fluctuations of daily light and nocturnal darkness. A clock in the brain synchronized to environmental cues generates biological changes that vary over a 24-hour cycle—circadian rhythms (from the Latin words *circa* and *diem,* meaning "about" and "a day," respectively). In this way, the earth's rotation is reproduced in the dynamics of our neuronal circuits.

The sleep-wakefulness cycle is a typical circadian rhythm. Wakefulness is characterized by sensory activity and movement; during sleep the senses lose touch with their surroundings, and movements subside. This periodic loss of consciousness appears on electroencephalogram (EEG) recordings as a clear signature: deep sleep consists of slow oscillations of high amplitude. Wakefulness, in contrast, is made up of fast, low-amplitude oscillations. Much about sleep remains a mystery, however. Why would an animal shut down basic sensory and motor activity for hours on end, leaving itself a target for predators? This question becomes more acute in aquatic mammals, which need to regulate breathing and body temperature while they sleep.

Remarkably, some animals have solved this problem by developing the ability to sleep with one half their brain while remaining vigilant with the other—a behavior known as unihemispheric slow-wave sleep (USWS). Still others engage in USWS under some circumstances but put both hemispheres to bed when necessary. Marine mammals, bird species and possibly reptiles enter a half-on/half-off state, sometimes keeping one eye open during these intervals. Recently researchers have even discovered a vestigial form of unihemispheric sleep in humans.

Half-slumber provides a fascinating vista into the science of sleep. While studies are carried out on the dormant half, the opposite side can serve as the requisite control for experiments. The ability to thrive with a relative lack of sleep, as dolphins and some birds do,

IN BRIEF

During sleep senses lose touch with their surroundings, and movements subside. This interlude raises the question of why any animal would shut down basic brain activities for endless hours, leaving itself a ready target for predators.

Some animals have solved this problem by developing the ability to sleep with one half of their brain while remaining vigilant with the other—an in-between state that goes by the name of unihemispheric slow-wave sleep.

Half-slumber provides a compelling means to study the science of sleep. Research can be carried out on the dormant half of the brain, while the other side becomes a control for experiments. This work may even help us understand human sleep disorders.

may provide ideas for treating human sleep disorders, which often affect one brain hemisphere more than the other.

ASLEEP BUT NOT REALLY

THE STUDY OF UNIHEMISPHERIC SLEEP started in 1964, when controversial researcher John C. Lilly suggested that dolphins could sleep using one side of the brain after observing that the animals keep only one eye closed during their daily rest. Lilly assumed that when asleep, dolphins could still watch and listen to their surroundings. It would take later experiments to determine what was happening in cetacean brains.

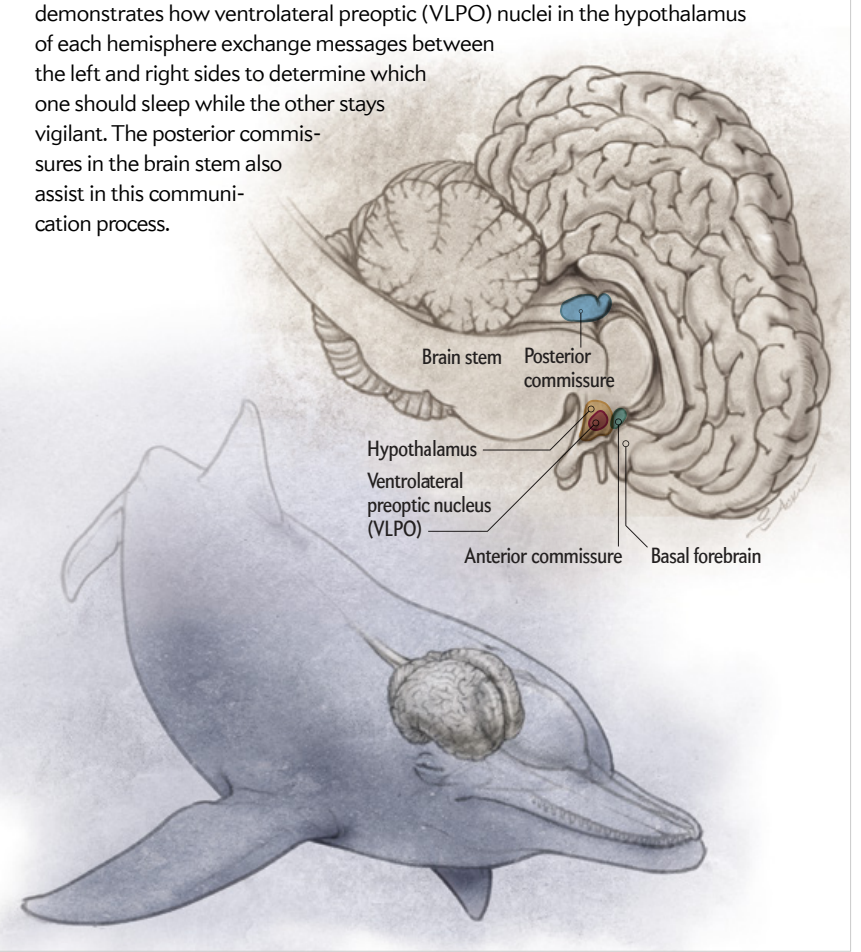
Cetaceans—whales, dolphins and porpoises—are still the subjects of studies on unihemispheric sleep. The animals preserve two physiological features from their ancestors' life on land: lungs for breathing air and mechanisms for maintaining nearly constant body temperature in water (thermoregulation). Sleeping with half a brain, it seems, has allowed them to retain those features in an aquatic environment.

More recently, Lev Mukhametov of the A. N. Severtsov Institute of Ecology and Evolution at the Russian Academy of Sciences and his colleagues looked more deeply than Lilly did into what was happening in the cetacean brain. Mukhametov and his colleagues studied sleep extensively in bottlenose dolphins. In EEG recordings, the researchers consistently found that one hemisphere of the animals' brain was in a state of slow-wave sleep, while the other was awake. They rarely observed sleep in both hemispheres (which is called bihemispheric slow-wave sleep, or BSWS), and they recorded no unequivocal signs of the rapid eye movement (REM) sleep associated with dreaming.

During USWS the awake hemisphere of a dolphin's brain controls swimming and surfacing to breathe. As Lilly surmised from cursory observation, the animal's one open eye, linked to the contralateral awake hemisphere of the brain, allows a dolphin to monitor for predators and swim in unison with its companions while the other half of the brain rests. In 1999 P. Dawn Goley of the department of biological sciences at Humboldt State University observed—as did Guido Gnone of the Aquarium of Genoa in Italy and his colleagues in 2001—that when dolphins swam in groups, the open eye of a pod member maintained visual contact with others. If a partner shifted to the opposite side, the eye pattern reversed.

Half On, Half Off

Diverse brain regions, including the brain stem, the hypothalamus and the basal forebrain, interact during the sleep-wake cycle. In dolphins, careful coordination between the left and right brain hemispheres allows one side to sleep while the other rests. A 2012 model of unihemispheric sleep from the University of Sydney demonstrates how ventrolateral preoptic (VLPO) nuclei in the hypothalamus of each hemisphere exchange messages between the left and right sides to determine which one should sleep while the other stays vigilant. The posterior commissures in the brain stem also assist in this communication process.



Dolphins also confront cold water temperatures that expose them to high heat loss. Keeping one hemisphere of the brain awake during rest allows the animals to stay warm by frequently moving their flippers and tail to swim and hover near the surface while they sleep—observations reported by Praneshri Pillay and Paul R. Manger, both then at the University of the Witwatersrand, Johannesburg.

We know that in cetaceans and other animals, the overall sleep-wake cycle is governed by interactions among multiple brain structures, including the brain stem, the hypothalamus and the basal forebrain. Precisely what regulates unihemispheric sleep remains a mystery, although we have clues. In 2012 David J. Kedziora and his colleagues at the University of Sydney worked out a mathematical model of USWS intended to represent dolphin sleep habits. In it, sub-

Illustration by Shiz Aoki and Jerry Gu, Anatomize Studios

structures within the hypothalamus in each hemisphere—the ventrolateral preoptic nuclei—exchange messages to regulate when sleep occurs in each hemisphere. It appears that inhibitory signals transmitted between the two hemispheres could allow one side to go to sleep while the other stays awake. Deep-brain structures, such as the posterior commissures in the brain stem, would also be involved. (The posterior commissures are extremely large in dolphins, giving rise to questions about their role in managing sleep.) The University of Sydney model gives neuroscientists a way to explore the mechanisms of how the brain hands off the delicate task of allocating sleep to one hemisphere or another.

Environmental cues also seem to play a role. Because the sleep-promoting neurons in the hypothalamus are thermosensitive, a rise or fall in brain temperature causes a corresponding fluctuation in the firing rate of these neurons. Indeed, in 1982 Mukhametov and his colleagues found that during USWS dolphins' brain temperatures decreased in the sleeping hemisphere and remained constant in the awake one.

When immersed in water, northern fur seals sleep with one brain hemisphere while adopting a body posture that allows them to breathe and stay alert for approaching predators.

A SINGULAR ADAPTATION

CETACEANS EVOLVED from a common terrestrial ancestor with hippopotamuses and other hoofed mammals. The move from a terrestrial to an aquatic environment was gradual and may have included a semiaquatic transition that entailed significant physiological and behavioral adjustments. Consequently, cetaceans' sleep behavior represents a singular example of adaptation to a new environment that demonstrates a trade-off between the need for sleep and survival.

Other animals make similar compromises. Seals, for example, have adopted various evolutionary solutions to the closely related problem of breathing and sleeping in water and on land. Some families of seals eschew USWS altogether. It has not turned up in earless, or "true," seals (the family Phocidae), including harp and elephant seals.

Northern fur seals (the family Otariidae), however, demonstrate a different story. In 2017 Oleg I. Lyamin of the A. N. Severtsov Institute of Ecology and Evolution reported that unlike dolphins, which appear to rarely experience BSWS and perhaps never enter REM sleep at all, northern fur seals undergo multiple sleep types, including BSWS, REM and USWS, in both their aquatic and terrestrial lairs. On land, BSWS predominates. In water, the amount of time spent in USWS increases, compared with that on land. REM sleep in water diminishes or even disappears.

When immersed in water and experiencing USWS, fur seals adopt a body posture that allows them to sleep, breathe and track approaching predators: they lie on one side with one flipper in the water and paddle continuously with it while keeping their other three flippers in the air to reduce heat loss. Their nostrils, meanwhile, remain out of the water so the seals can breathe. The brain hemisphere on the opposite side from the moving flipper (and the one open eye) is awake, letting the animals issue motor commands for paddling and retaining postural stability. On land, USWS allows fur seals to watch for predators and coordinate activity with companions, but it does not help with breath control, body temperature or coordination of movement.

Some birds, too, engage in unihemispheric sleep as they balance the need for rest and defensive alertness. (At times, USWS is combined with BSWS and REM.) In 1996 Jadwiga Szymczak, then at Nicolaus Copernicus University in Poland, recorded the presence of slow-wave EEGs in one hemisphere of the European black bird. And in 2001 Niels C. Rattenborg, then at the department of life sciences at Indiana State University, and his colleagues did the same in pigeons. Similarly, in 1999 Rattenborg had found that mallard ducks sleep with only half a brain to watch for threats. Ducks that kept one eye open while stationed at the outside edges of a group showed 150 percent higher levels of USWS than birds located toward the center. The open eyes of the "sentinel" ducks were directed away from the group. Mark A. Elgar, now at the University of Melbourne in Australia, reported in a 1989 study that vigilance decreases when the group grows larger and when an animal moves toward the center of the group.

Migrating birds during nonstop, long-distance flights also rely on differing sleep strategies. In 2016 Rattenborg, now at the Max Planck Institute for Ornithology in Seewiesen, Germany, and his team studied USWS and BSWS in great frigate birds (*Fregata minor*) during their 10-day sojourns. In a single USWS episode, one hemisphere showed a waking EEG pattern contralateral to the direction of a flight turn, indicating that the open eye on the opposite side was watching where the flock was headed. Also, Thomas Fuchs, then at Bowling Green State University, discovered in 2006 that Swainson's thrush compensates for

the loss of sleep during night flight by increasing total sleep time, taking daytime micro naps and, when perching, closing one eye.

WHAT ABOUT US?

HUMANS DO NOT ENGAGE in classic USWS, but they occasionally experience something reminiscent of it. Masako Tamaki and her group at Brown University made EEG recordings when people spent the night in an unfamiliar environment. In a 2016 publication by Tamaki, the EEGs showed slow waves indicative of deep sleep in the right hemisphere and shallow slow-wave activity in the left hemisphere, a sign of more alertness. The left hemisphere, moreover, was more easily aroused than its opposite half. This asymmetry, referred to as the first-night effect, disappears by the second night but seems to preserve vigilance in an unfamiliar place. It is reminiscent of mothers who retain a low awakening threshold to cries or other noises they identify as coming from their babies.

We may feel the sleep debt after the first night away from home. But other animals that sleep with one side of the brain all the time seem to be well adapted to their routines. Those that immerse themselves in USWS spend less time sleeping, compared with those that engage in BSWS or REM sleep.

Even so, their ability to swim, fly, eat or socialize with companions remains undiminished. Dolphins spend almost two thirds of their day awake and the rest of the time in USWS, trading off sleep time between the two hemispheres. Brain and body recovery, however, does not appear to be affected, despite the absence of REM sleep.

In 1997 Mukhametov and his colleagues reported that dolphins in sleep studies always appeared to be in good health. In captivity, where scientists could observe the animals closely, dolphins learned and memorized complex tasks. Frigate birds sharply reduced total sleep while flying but maintained a high level of attention and efficient flight performance during their extended journeys.

Some animals seem to cope by sharing the half-sleep burden. Mallard ducks that act as flock sentinels by keeping one eye open lose sleep but without impaired behavior. The birds later pass off their lookout roles to a companion on another day. Unihemispheric sleep continues to fascinate the research community because it illustrates the diverse evolutionary strategies that have emerged to allow animals to get their rest every day.

The interest generated in USWS from field experiments has even made it into a laboratory tool for exploring the role of sleep in helping to shape development of the brain just after birth. In 1999 my group in the department of general psychology at the University of Padova in Italy found that just-born chickens (*Gallus gallus*) experienced significantly more left-hemisphere sleep during the first week after hatching. The chicks favored that hemisphere in those early days to learn about stimuli—patterns and colors—that must be processed for the first time by their new brain: sleep appeared to play a role in organizing what they had just learned.

Right-hemisphere sleep increased in the chicks as activity such as spatial analysis and the processing of new events prevailed on that side in the second week. When we trained chicks in a color-discrimination task, they subsequently registered more left USWS (with their right eye closed and their left hemisphere asleep) because that hemisphere was dominant in learning about colors. Chicks used the left eye for a spatial-learning task that required them to select one of four containers in a particular corner of their enclosure. They had to pick the container with a hole on top that contained a food treat. When they were done, chicks showed more right USWS (with their left eye closed and their right hemisphere sleeping) to rest the side of the brain that specializes in this type of task.

The most active hemisphere—whether engaged in USWS or BSWS—spent relatively more time sleeping to allow for recovery. Meanwhile the open eye on the side of the nondominant hemisphere took over to watch for predators and to stay apprised of the environment. In fact, moving a dark object over the cage during USWS caused chicks to wake immediately, startle and emit distress calls. Vigilance remained intact, but it did not detract from sleep as a time to sort out the intense sensory experiences of the birds' first days in a new world.

Ultimately studying animals that sleep with half a brain could aid us in understanding the continuing biological enigma of sleep—and perhaps even sleep problems in humans. Apnea and other disorders sometimes have effects more in one hemisphere than the other. This work may help answer how a species balances the benefits of rest with a need to protect itself against a hungry predator. Sleeping with one side of the brain is a brilliant answer to this dilemma, enabling an animal to experience conscious and unconscious states all at once. Research on unihemispheric sleep resonates through the millennia with a frequently quoted passage from Heraclitus' *Fragments:* "Even a soul submerged in sleep is hard at work and helps make something of the world." SA

MORE TO EXPLORE

Cetacean Sleep: An Unusual Form of Mammalian Sleep. Oleg I. Lyamin et al. in *Neuroscience & Biobehavioral Reviews,* Vol. 32, No. 8, pages 1451–1484; October 2008.

Physiologically Based Quantitative Modeling of Unihemispheric Sleep. D. J. Kedziora et al. in *Journal of Theoretical Biology,* Vol. 314, pages 109–119; December 7, 2012.

Unihemispheric Sleep and Asymmetrical Sleep: Behavioral, Neurophysiological, and Functional Perspectives. Gian Gastone Mascetti in *Nature and Science of Sleep,* Vol. 8, pages 221–238; 2016.

Evidence That Birds Sleep in Mid-Flight. Niels C. Rattenborg et al. in *Nature Communications,* Vol. 7, Article No. 12468; August 3, 2016.

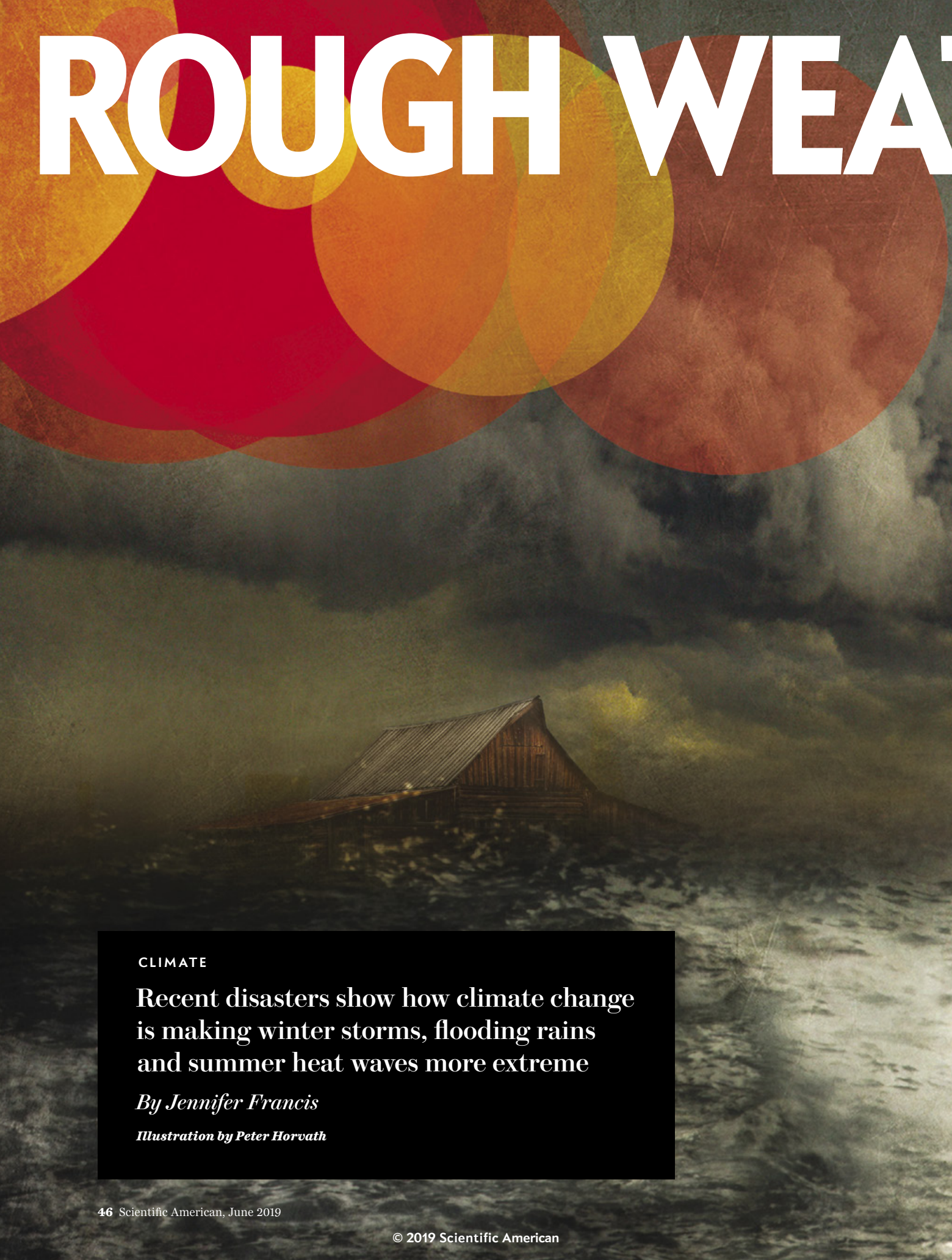
Sleep in the Northern Fur Seal. Oleg I. Lyamin et al. in *Current Opinion in Neurobiology,* Vol. 44, pages 144–151; June 2017.

FROM OUR ARCHIVES

Sleeping with Half a Brain. Christof Koch; September 2016.

scientificamerican.com/magazine/sa

ROUGH WEA



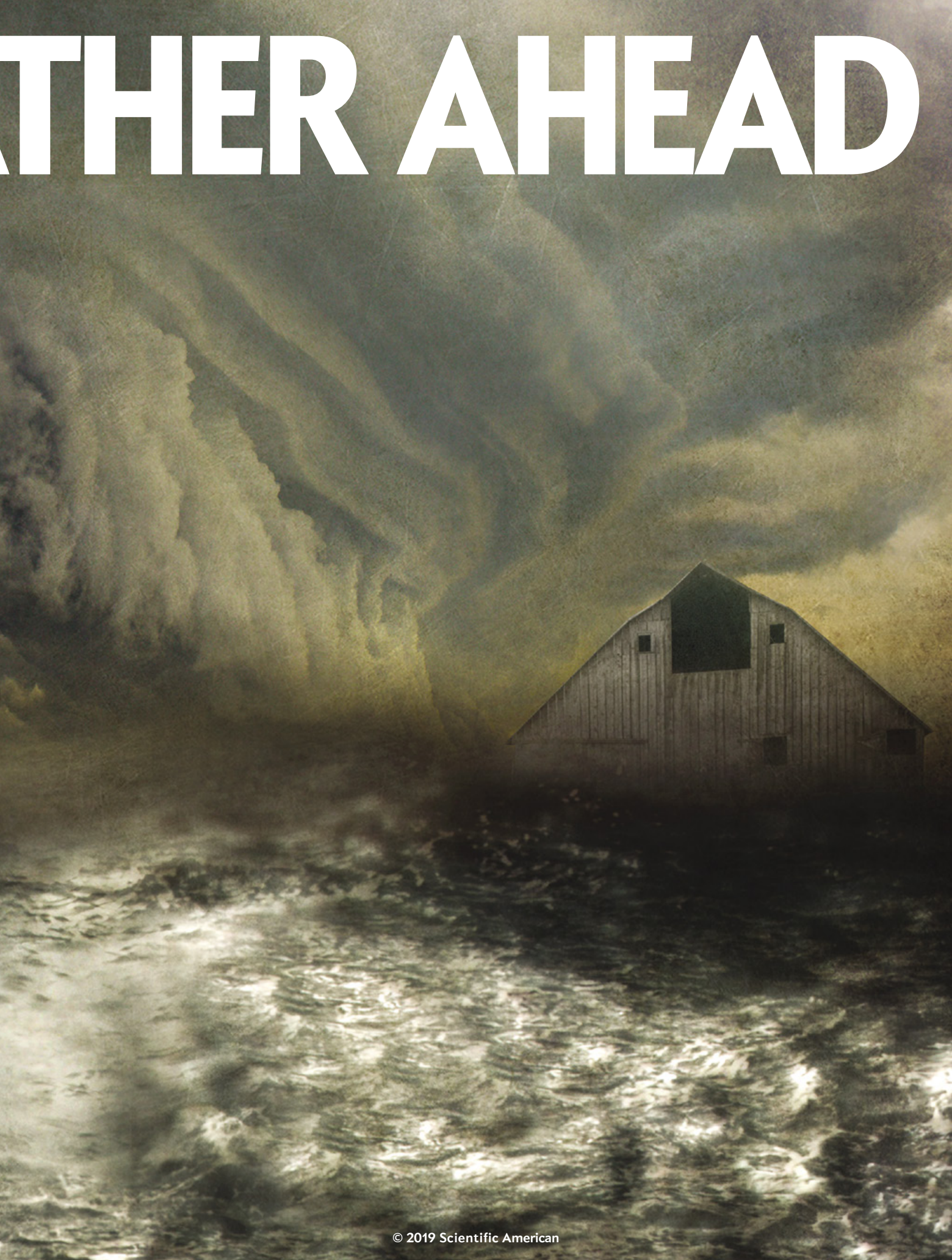
CLIMATE

Recent disasters show how climate change is making winter storms, flooding rains and summer heat waves more extreme

By Jennifer Francis

Illustration by Peter Horvath

THER AHEAD



Jennifer Francis is a senior scientist at the Woods Hole Research Center in Falmouth, Mass. She was a research professor at Rutgers University from 1994 to 2018. Francis serves on *Scientific American*'s board of advisers.

SHE WAS BORN IN THE USUAL way. A disorganized blob of clouds emerged over the Atlantic Ocean off Africa's bulging western coast, just north of the equator. Atmospheric pressure there was low, typical for late summer. Natural variability in the earth's climate spawns tropical disturbances every year in this area—sometimes more, sometimes fewer, and sometimes they become hurricanes. Weather forecast models unanimously predicted that the clouds would coalesce into a storm that curved harmlessly northwest into the mid-Atlantic, far from land.

On September 1, 2018, tropical storm Florence began to do just that but then turned stubbornly westward while becoming better organized, seemingly aimed at the Caribbean. Another worrisome disturbance was already lurking near Puerto Rico, which was still reeling from Hurricane Maria's devastation a year before. Three major cyclones were also spinning in the tropical Pacific, fueled by ocean temperatures that were off the charts. The mob of storms drew energy from record-warm ocean temperatures, which have risen steadily since the 1970s in lockstep with increasing atmospheric temperatures, driven by heat-trapping greenhouse gases—global effects of climate change. Storms feed off ocean heat and water vapor in the atmosphere, which is climbing as well.

Conflicting factors kept Florence weak, however. Although that seemed fortunate, it provoked anxiety among forecasters. Weaker storms are more readily steered by lower-altitude winds, and those winds were blowing east to west, straight at the U.S. East Coast. They were skirting the southern rim of a big, circular, unusually strong high-pressure center parked in the middle of the North Atlantic. High-pressure centers arise naturally, but evidence shows that some are getting stuck in place more often, a regional symptom of a warmer climate. A "blocking high" like this one had steered Hurricane Sandy on its bizarre path from the Atlantic into New Jersey in 2012.

On September 4 something unexpected happened: weak Florence moved over a spot in the west-central Atlantic that was abnormally warm. Fueled by that warmth, she rapidly intensified to a Category 4 hurricane and at a nearly record-breaking northerly latitude. Random hot pools of ocean water are another regional effect of our changing climate.

As Florence churned, the forecast models began to coalesce: she seemed likely to hit the coastal Carolinas and stall, where she could unleash deep flooding as Hurricane Harvey had done a year earlier over Houston. Sure enough, Florence struck the coastal Carolinas on September 14 and sat for four days. The low-altitude steering winds were now too weak to move the system. Florence dropped more than 30 inches of rain in places and reportedly killed more than 50 people and millions of animals (mostly chickens) while racking up an estimated $20 billion or so in losses. Floodwaters passing through factory farms, mines and sewage-treatment plants polluted rivers and estuaries for weeks.

Florence's wrath will not soon be forgotten, and neither will the blatant demonstration of climate change in action. The hurricane's unusual severity can be attributed to specific effects of climate change: greater heat in the air and ocean, extra water vapor, the tenacious blocking high and weak steering winds. These factors are in play around the world, favoring rapid storm intensification, heavier precipitation, greater flooding and stronger storm winds.

Florence was just one of many examples in 2018 of the various ways climate change is affecting extreme weather. Multiple "bomb cyclones" battered the northeastern U.S. An outbreak of Arctic air called the "beast from the east" froze Europe. Severe heat waves crippled Japan, Scandinavia and Greece. Floods ruined parts of Venice, Paris and Maryland.

Such misfortunes have happened since humans walked the earth, of course. But every year it becomes clearer that today's epidemic of bizarre weather cannot be explained by natural variability. Although in the past scientists were careful to not directly link climate change to specific weather events, we are now indeed saying that because of climate change, major floods are occurring more often. Killer heat waves are hotter and lasting longer. Cold spells are sticking around longer in some places, too.

How much of our daily wild weather, which in 2018 caused more than $160 billion in losses worldwide, can be blamed on changing climate? The answer depends on untangling the roles of three broad factors. First is the global effect of more heat in the ocean and more heat and vapor in the atmosphere. The water va-

IN BRIEF

Scientists can now show that specific extreme weather events are made worse by climate change, not just natural climate variability.

Global climate change factors include more heat in the world's oceans and more heat and vapor in the atmosphere.

Regional factors include an expanding tropical zone, a "cold blob" in the Atlantic Ocean and a disrupted polar vortex; all can interact with natural variability.

WILDFIRE burns in Kårböle, Sweden, in July 2018, magnified by abnormal heat and drought (*1*). In September 2018 an immovable high-pressure center traps Hurricane Florence above the eastern U.S. for days, flooding towns such as Lumberton, N.C. (*2*).

MATS ANDERSSON *Getty Images (1);* JOE RAEDLE *Getty Images (2)*

por story deserves more attention than it gets: vapor is another greenhouse gas that traps heat, it releases even more heat when it condenses into clouds, and it feeds precipitation from storms.

The second factor is regional effects, such as stubborn, blocking high-pressure centers, expanses of melting sea ice, a growing "cold blob" of ocean water south of Greenland, a slowing Gulf Stream and an increasingly disrupted polar vortex.

The third involves the complicated ways that natural variations, such as El Niño and La Niña, interact with the regional factors. Research into this interplay is cutting-edge, controversial—and bearing fruit. We now understand better how and why climate change is escalating extreme weather, revealing how we will need to prepare for increasingly frequent and intense dangers.

A NASTY NOR'EASTER

THE EARTH'S ATMOSPHERE is a cloak of roiling gases. Air constantly heats and cools, with the sun pouring in energy during the day and warm surfaces radiating it back to space at night. Uneven heating creates local winds that blow every which way. Water is continuously evaporating from land and sea, condensing in the air and falling down as rain or snow.

Yet within this chaos are remarkably predictable patterns governed by latitude, the earth's spin, mountain ranges, ocean circulations and other influences. In the Atlantic, hurricanes like Florence form in the eastern tropics and move westward. In the Pacific, tropical storms move westward, too. A polar jet stream blows from west to east around the Northern Hemisphere at a latitude near the U.S.-Canada border; another polar jet in the Southern Hemisphere crosses the lower reaches of South America and Africa. More cyclical are large wind systems linked to ocean-temperature fluctuations, such as El Niño and La Niña, which wax and wane every three to eight years and affect winds and precipitation worldwide. Data from cores of mud extracted from various seabeds show these patterns have held for hundreds of thousands of years.

Chaos and consistency also prevail in the oceans, over longer cycles, amid constant heating, cooling and flowing waters. The Pacific Decadal Oscillation is a seesawing of warm and cold temperatures between the eastern and western North Pacific Ocean, each phase persisting for about a decade. The Atlantic Meridional Overturning Circulation is a slow current of warm, salty surface water that heads north in the western Atlantic, then loses heat, dives deep and flows back south to Antarctica. A round-trip through this circuit takes about 1,000 years.

Interactions between the atmosphere and oceans introduce natural variability into climate. Some years are hotter or colder in certain regions; some years are wetter or drier. But those same mud-core data from past millennia show that the variability has limits: the climate rarely exceeds certain bounds. Until now.

I experienced one of those exceptions firsthand in the late winter of 2018. March is supposed to roar in like a lion, but this was ridiculous. Mother Nature was delivering a parade of potent nor'easters—storms that churn just off the Atlantic Coast, lashing the Eastern Seaboard with winds from the northeast. The three climate change factors—higher heat and vapor globally, regional effects, and the interplay between natural variability and those effects—are goosing these storms.

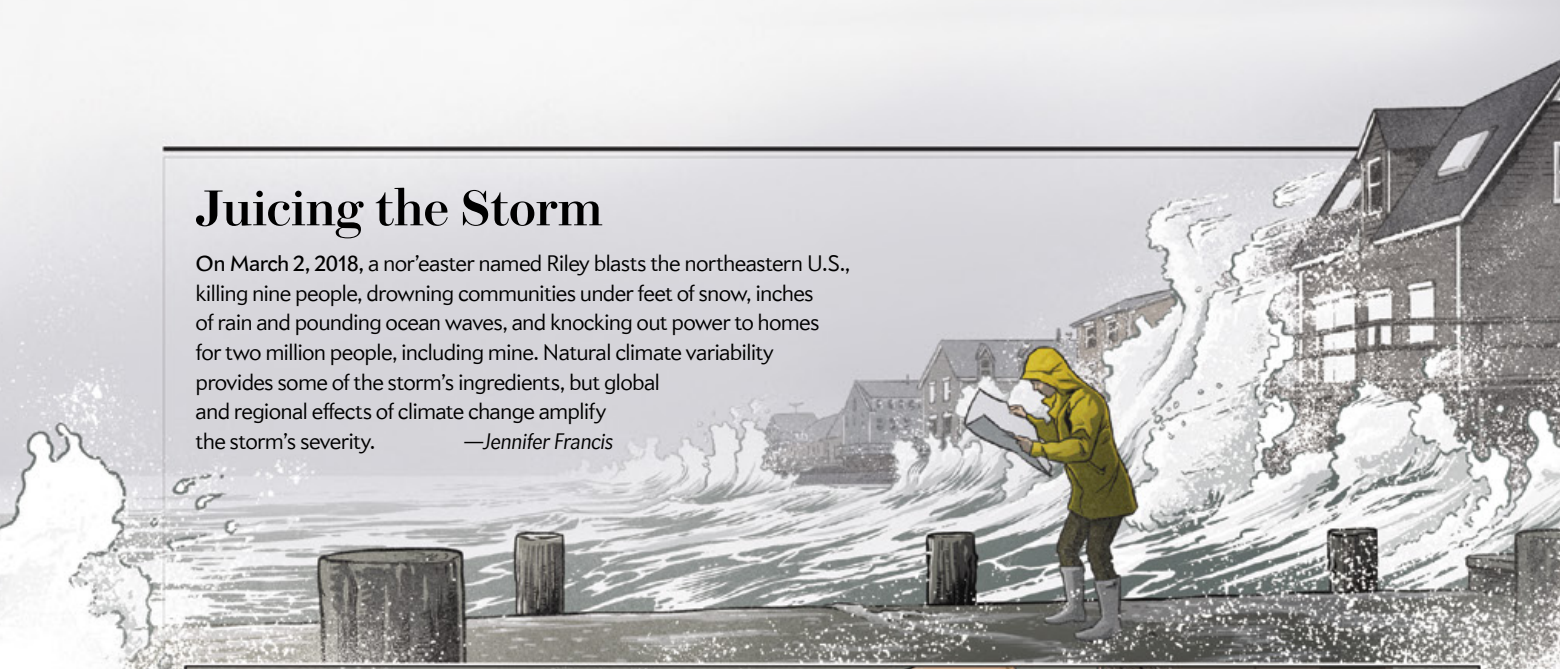
I was anxiously monitoring the latest forecast models. They showed a seemingly innocuous wiggle in the jet stream over the North Pacific, and they agreed that it would cross to the Atlantic Seaboard and spawn a whopper of a storm aimed at our coastal town in southeastern Massachusetts. The models were bullish about a blizzard developing quickly—technically a bomb cyclone—and dumping its snow right on my neighborhood. It would be the third major nor'easter of the season, which is unusual.

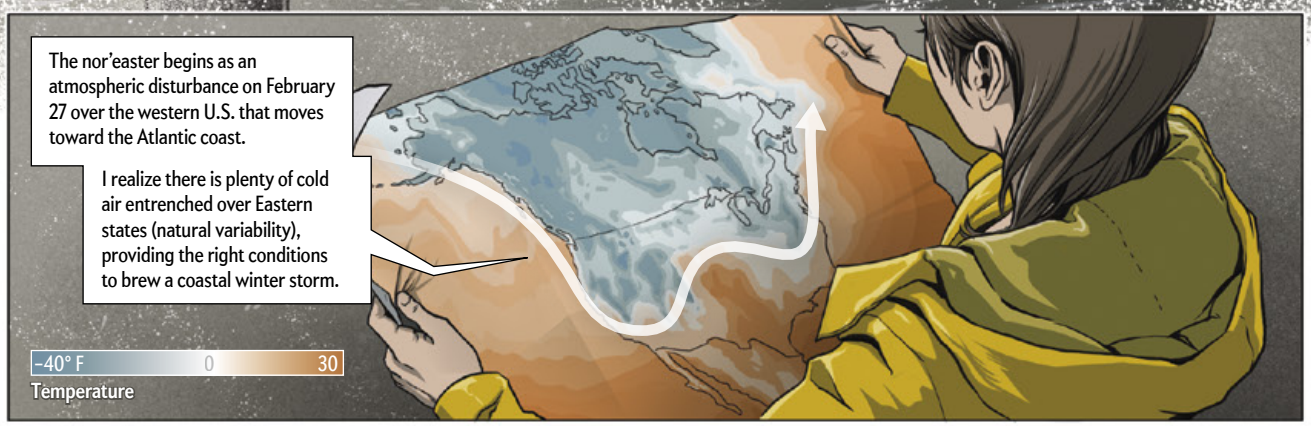
All the ingredients were in place. Cold air was entrenched over Eastern states (a naturally occurring factor). Extra heat in the ocean (a global factor) provided ample energy and moisture for a mounting storm. Water temperatures in the Atlantic off New England were far above normal (a regional factor).

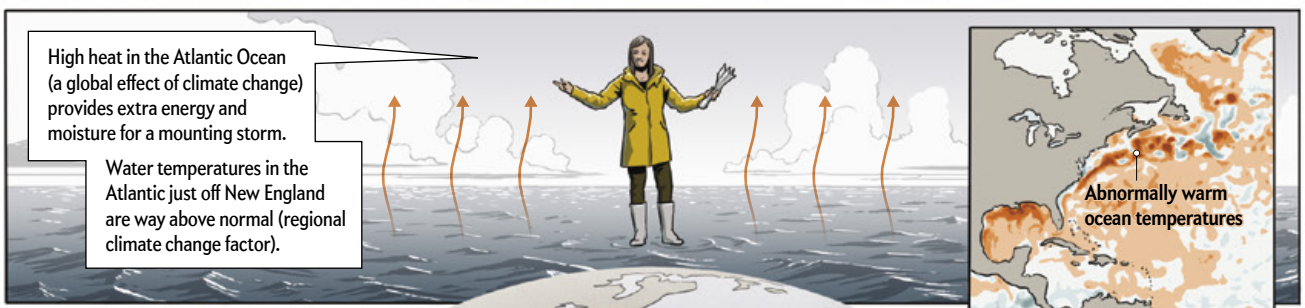
The interplay between natural and regional factors was another important ingredient. In late 2013 the Pacific Decadal Oscillation flipped from its so-called negative phase to a positive phase, in keeping with its natural cycle. It raised sea temperatures above

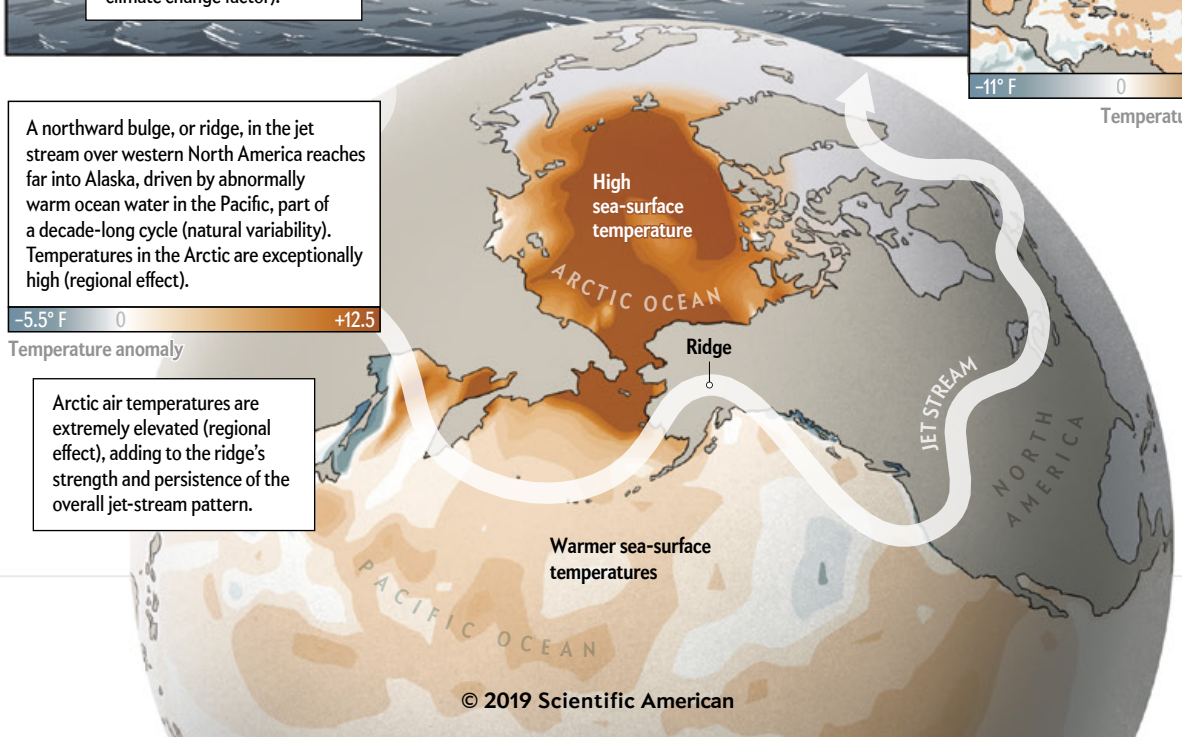
Juicing the Storm

On March 2, 2018, a nor'easter named Riley blasts the northeastern U.S., killing nine people, drowning communities under feet of snow, inches of rain and pounding ocean waves, and knocking out power to homes for two million people, including mine. Natural climate variability provides some of the storm's ingredients, but global and regional effects of climate change amplify the storm's severity. *—Jennifer Francis*

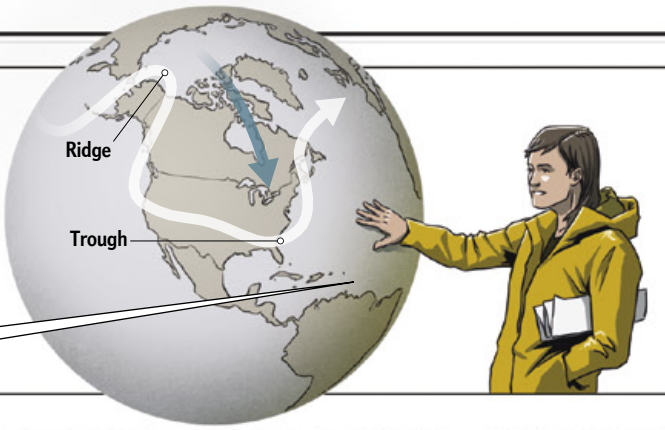




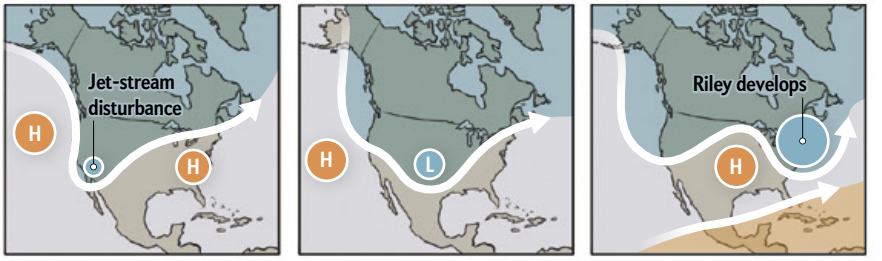


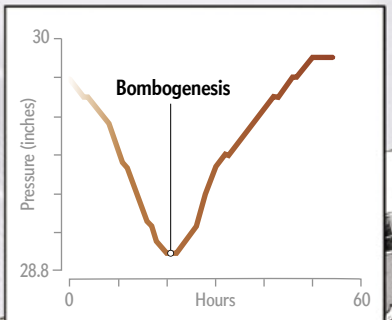


The strong ridge leads to a large southward trough that extends over most of eastern North America. It allows frigid Arctic air to plunge down, creating an abrupt temperature contrast with the warm Atlantic coast waters (regional effect).



The disturbance in the jet stream (a small wave in the larger ridge-trough pattern) moves east and flattens, but when it hits the strong air-temperature contrast along the East Coast, it strengthens again (regional effect) and picks up extra energy from a subtropical jet stream that is blowing across the southern U.S. (natural variability).





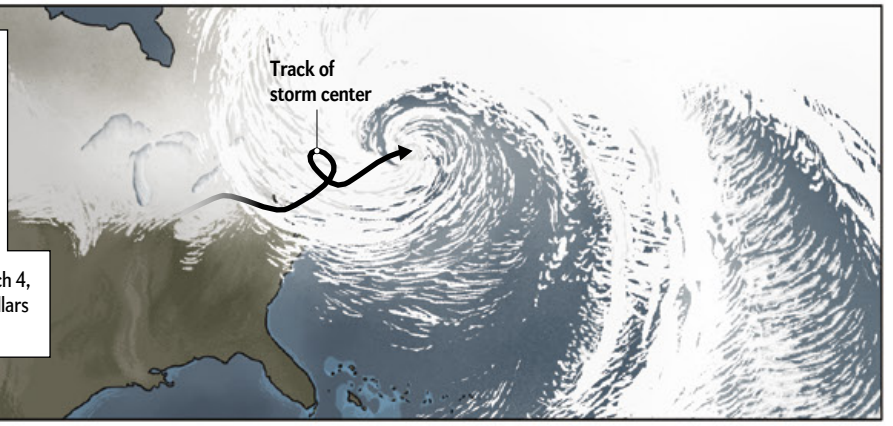
National Weather Service data for the developing storm near my location on March 1 reveal that "bombogenesis" is about to happen—when a storm's atmospheric pressure drops sharply and quickly—causing Riley to "explode" in size and strength (regional effect).

Riley's 80-mph winds lash New England on March 2, knocking down trees and power lines across a wide area. Heavy rain drenches some areas; snow falls at three inches per hour in others.

Ocean waves 15 feet high pummel houses along east-facing shores in Massachusetts.

The intense storm stalls offshore of New England for two more days instead of moving on, pumping out more wind, rain, snow and battering seas. A blocking high-pressure center near Greenland thwarts its movement—yet another regional effect of climate change that is happening more often in the North Atlantic.

Riley finally departs on March 4, leaving behind billions of dollars in damage.



SOURCES: NATIONAL OCEANIC AND ATMOSPHERIC ADMINISTRATION (*jet stream and Pacific Ocean temperature in fourth panel, data in fifth and sixth panels and storm track in eighth panel*); UNIVERSITY OF MAINE (*temperature data in second and third panels and Arctic air temperatures in fourth panel*); NATIONAL WEATHER SERVICE (*bombogenesis graph*)

Illustration by Matt Twombly

average along the western coast of North America. Extra heat pumped into the atmosphere from this warm water favors the formation of a northward bulge (called a ridge) in the jet stream over western North America that can extend into Alaska.

That is where interaction with a regional effect comes into play. Air temperatures in the Arctic have risen two to three times faster than the rest of the planet, especially in winter. The extraordinary loss of 75 percent of the Arctic's sea-ice volume in only 40 years is responsible for most of this warming. The Pacific ridge can tap into this extra warmth, causing it to intensify and stick around for a long time. This so-called Ridiculously Resilient Ridge is largely responsible for the extended drought and heat waves that set the stage for recent severe wildfires along the U.S. West Coast.

A strong ridge is usually accompanied by a large southward dip (called a trough) to the east of it, which in this case was over eastern North America. A deep trough allows cold Arctic air to plunge far southward, creating a stark temperature contrast with the warm Atlantic waters along the East Coast. The atmosphere despises temperature contrasts. It generates storms to mix air masses in an attempt to even out the differences; bomb cyclones are an intense example of this process. This ridge-and-trough pattern tends to spawn nor'easters, and it has become increasingly prevalent in recent winters.

Sure enough, National Weather Service data painted a scenario of "bombogenesis"—when a storm's atmospheric pressure drops more than 24 millibars in 24 hours, causing it to "explode" in size and power. My neighborhood was in the crosshairs. As dusk arrived on March 2, so did the nor'easter's howling wind, driving rain and snow, power outages, and major erosion from high waves and storm surges. Afraid that one of the tall white pines in our yard might fall on the house, my cat and I (my husband was away) opted to sleep on the living-room couch rather than in my upstairs bedroom. The wind roared so loudly overnight that I did not hear the crash of any of the 20 big trees that dropped around us, somehow missing our roof.

The storm took its sweet time leaving, as a blocking high-pressure center near Greenland thwarted its movement, ravaging half a dozen states with hurricane-force winds. The nor'easter killed at least nine individuals, knocked out power for more than two million people (five days in our town) and flooded coastal communities.

WICKED WINTER WEATHER

THE PARADE of destructive nor'easters was not the only winter weather in 2018 juiced by climate change. Parisians and Venetians suffered the worst flooding in half a century as a result of prolonged rainfall, while deadly windstorms struck Germany and northern France. Several feet of snow buried Davos, Switzerland, just as the well-heeled and high-heeled tried to arrive for the annual meeting of the World Economic Forum.

In North America, the big story was "weather whiplash"—sudden and dramatic shifts between long-lasting extremes. Although research is still sparse, evidence is accumulating that these exaggerated swings are occurring more frequently and that our three climate influences are in play.

Case in point: during three weeks of January, such bitter cold gripped the eastern U.S. that iguanas in southern Florida dropped from trees in near-frozen comas while residents in Western states basked in above-normal temperatures. Then in early February, weather whiplash struck. An abrupt reversal in the jet-stream pattern brought record-breaking warmth to hundreds of Eastern cities. Temperatures jumped more than 40 degrees Fahrenheit in 24 hours, bringing the iguanas back to life. At the same time, a deep chill settled over the Western states. In the atmospheric battleground between the eastern and western air masses, potent storms in the Mississippi Valley caused the worst flooding in decades. The frequency of heavy precipitation in that region has increased by about 40 percent since the 1950s.

Global, regional and interplay factors had struck again. Overall global warming and moistening certainly gave these extremes a boost. And the same regionally loopy jet stream that would contribute to the parade of bomb cyclones had set the stage. Winter whiplash slapped the U.S. and Canada in February 2019, too; in some areas, temperatures ricocheted by 50 or 60 degrees F and wind chills by more than 100 degrees F in only a few days.

Science is rapidly revealing that climate change can be blamed for amplifying extreme weather. Natural variability cannot explain what we already see and feel.

SCORCHING, SOAKING SUMMER

SUMMER 2018 also brought a smorgasbord of rough weather to the Northern Hemisphere, much of it exacerbated by climate change. While Japan, Texas and even Scandinavia baked for weeks, the U.S. Eastern Seaboard sloshed through its wettest season on record. Tenacious droughts plagued the western U.S., parts of Europe and the Middle East, contributing to a horrific spate of wildfires that cost $20 billion in California alone. Extreme summer conditions ruined crops, boosted toxic algae blooms, shut down nuclear-reactor cooling systems and triggered blackouts across four continents.

Some impacts were clearly related to the global factor. Higher average temperatures cause hotter heat waves. Extra water vapor feeds summer downpours and helps to raise nighttime temperatures by trapping additional heat near the surface. The exceptional heat plus humidity, especially at night, can be a deadly combination, making it difficult for the human body to cool itself through evaporation of sweat. Worldwide, thousands of people without air-conditioning died.

Less straightforward were climate influences on the summer jet stream—literally a "hot" research topic. What is already clear, though, is that both global and regional factors are involved in favoring an unusually wavy jet stream such as the one that engulfed Scandinavia in heat waves, drought and fire. Temperatures there from May through July broke records going back 260 years.

What role did regional changes play? During spring and sum-

mer, warming occurs across a band of land south of Canada and Russia's Arctic coasts. Spring snow cover has been melting there ever earlier. The loss of this highly reflective surface exposes the underlying soil to strong spring sunshine sooner, drying it out earlier. Dry soil warms much faster than damp soil, so temperatures climb. The warm-up gives summer a head start, shifting the jet stream northward sooner than usual, allowing warm air to penetrate high latitudes.

The band of abnormally warm land can help split the jet stream into two branches, a common occurrence during winter but less so in summer. Weather systems between the two often get trapped for long periods because there is little wind there to move them along. During the summer of 2018 the jet stream over Eurasia and North America was split much of the time, creating persistently warm, dry conditions in some areas, and prolonged rainy periods in others, that broke records on both continents.

FASTEN YOUR SEAT BELT

THE WILD WEATHER OF 2018 was a trailer for the main feature, coming to audiences everywhere as greenhouse gases continue to accumulate. Some of the consequences of global effects—warmer oceans, warmer air and increased atmospheric moisture—are obvious and direct. Intense research is focused on untangling the jumble of regional effects and their interplay with natural variability. Let's look at four examples.

Evidence suggests that the earth's tropical zone around the equator has been widening toward the poles. That pushes storm tracks poleward and makes some temperate regions hotter and drier. The clearest symptoms can be seen in the dry zones that define the northern and southern edges of the tropics, such as southern California, the Mediterranean and Australia, where more severe droughts and heat waves have captured headlines. Scientists are working to understand the likely contributors—warming, atmospheric dust and soot particles that alter air temperatures and cloud formation.

Another regional factor under scrutiny is the apparent slowing of the Gulf Stream, a major ocean current flowing from the Gulf of Mexico up the Eastern Seaboard, then across the North Atlantic toward the U.K. It is the surface branch of the larger Atlantic Meridional Overturning Circulation. A slowdown would upset weather patterns and fisheries on both sides of the ocean. Measurements of the subsurface ocean are sparse, but oddities in well-monitored surface temperatures, such as abnormal warmth along the East Coast and the blob of cool waters south of Greenland, provide important clues that this large-scale circulation system may indeed be slowing. A shift in ocean-temperature patterns will alter the strength and path of storms. A hyperactive North Atlantic storm track in recent years may be a response to a slowing Gulf Stream, along with feverish waters that most likely fomented the bomb cyclones of the winter of 2018.

Blocking high-pressure centers are another regional feature to watch. Observations suggest they are occurring more often in some places, such as over Greenland and western Russia, but atmospheric models struggle to predict the development and demise of these swirling eddies in the sky. Blocks can form for various reasons, some related to natural variability and some to climate change. The remnants of tropical storms, for example, can naturally inject surges of energy into the jet stream, causing it to buckle and spin off orphan eddies. As oceans warm, however, tropical storms may survive farther northward and later into the autumn season, increasing the likelihood of collisions with the jet stream that can create a block, which can then push hurricanes and other weather systems in unusual directions.

During October 2018, for example, Hurricane Leslie dawdled in the Atlantic for more than two weeks, finally going where no known hurricane has gone before: just west of Portugal. Strong winds and flooding rains pummeled the Iberian Peninsula. At the time, a strong block sat over northeastern Europe, creating the wavy jet-stream pattern that captured Leslie and carried it on a long journey across the Atlantic.

A final regional factor is the stratospheric polar vortex, which was in the news frequently in the winter of 2018—and again in the winter of 2019. It has been behaving oddly. This ring of strong winds circles a pool of frigid air over the North Pole only in winter, at an altitude of around 30 miles. Every few years the right conditions can deform the ring or even split it into two or more smaller rings, which tend to migrate southward, bringing severe cold spells with them. Simultaneously, warm air from the south invades the Arctic, creating topsy-turvy temperatures. During the split polar vortex in late January of this year, it was warmer near the North Pole than in Chicago. These so-called sudden stratospheric warming events can occur naturally, but lately they are happening more often. Several new studies have found that the dramatic sea-ice loss in the Arctic Ocean north of western Russia may help trigger these vortex disruptions. Those of us living in the midlatitudes may be attacked more frequently by the polar vortex as global warming intensifies.

Although certain aspects of the uncontrolled experiment we are forcing on the earth's climate remain elusive, science is rapidly revealing that climate change can be blamed for amplifying extreme weather and its consequences. Understanding the links will help us see the future more clearly and prepare for the impacts on agriculture, international security, marine life, forests, freshwater resources, infrastructure and human health. The effects are already apparent and will only worsen.

Yet there is reason for hope. The rash of bad weather has shined a bright light on the well-funded campaign to spread disinformation and generate doubt about climate change among the public. Despite what the doubters say, natural variability simply cannot explain the extremes we already see and feel. Recent surveys show most people finally accept that climate change is real and caused by us. Insurers, military leaders, property developers and municipal administrators are responding to the tangible risks to life and property. Perhaps we are finally ready to confront the rough ride ahead. SA

MORE TO EXPLORE

More-Persistent Weak Stratospheric Polar Vortex States Linked to Cold Extremes. Marlene Kretschmer et al. in *Bulletin of the American Meteorological Society,* Vol. 99, No. 1, pages 49–60; January 2018.

Observed Fingerprint of a Weakening Atlantic Ocean Overturning Circulation. L. Caesar et al. in *Nature,* Vol. 556, pages 191–196; April 12, 2018.

Re-examining Tropical Expansion. Paul W. Staten et al. in *Nature Climate Change,* Vol. 8, pages 768–775; September 2018.

FROM OUR ARCHIVES

Rethinking the Gulf Stream. Stephen C. Riser and M. Susan Lozier; February 2013.

scientificamerican.com/magazine/sa

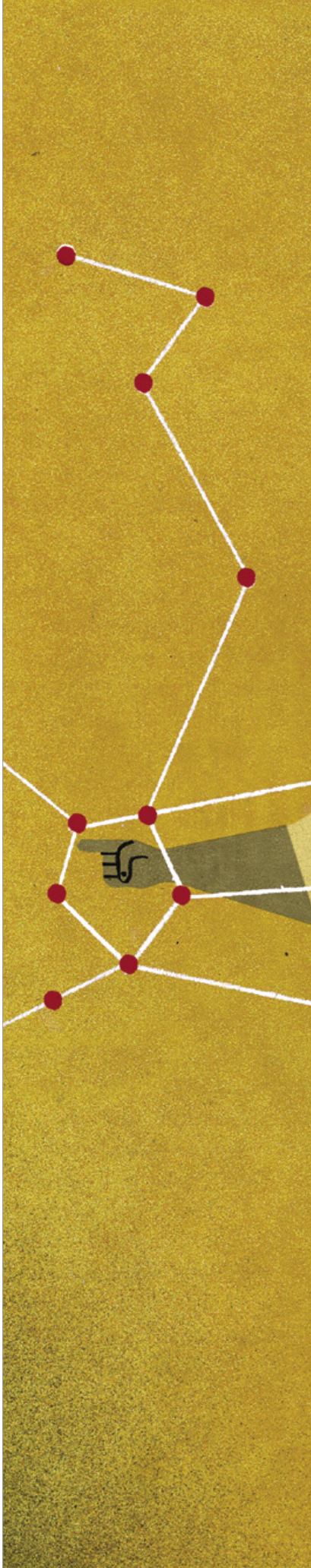
IMMUNOLOGY

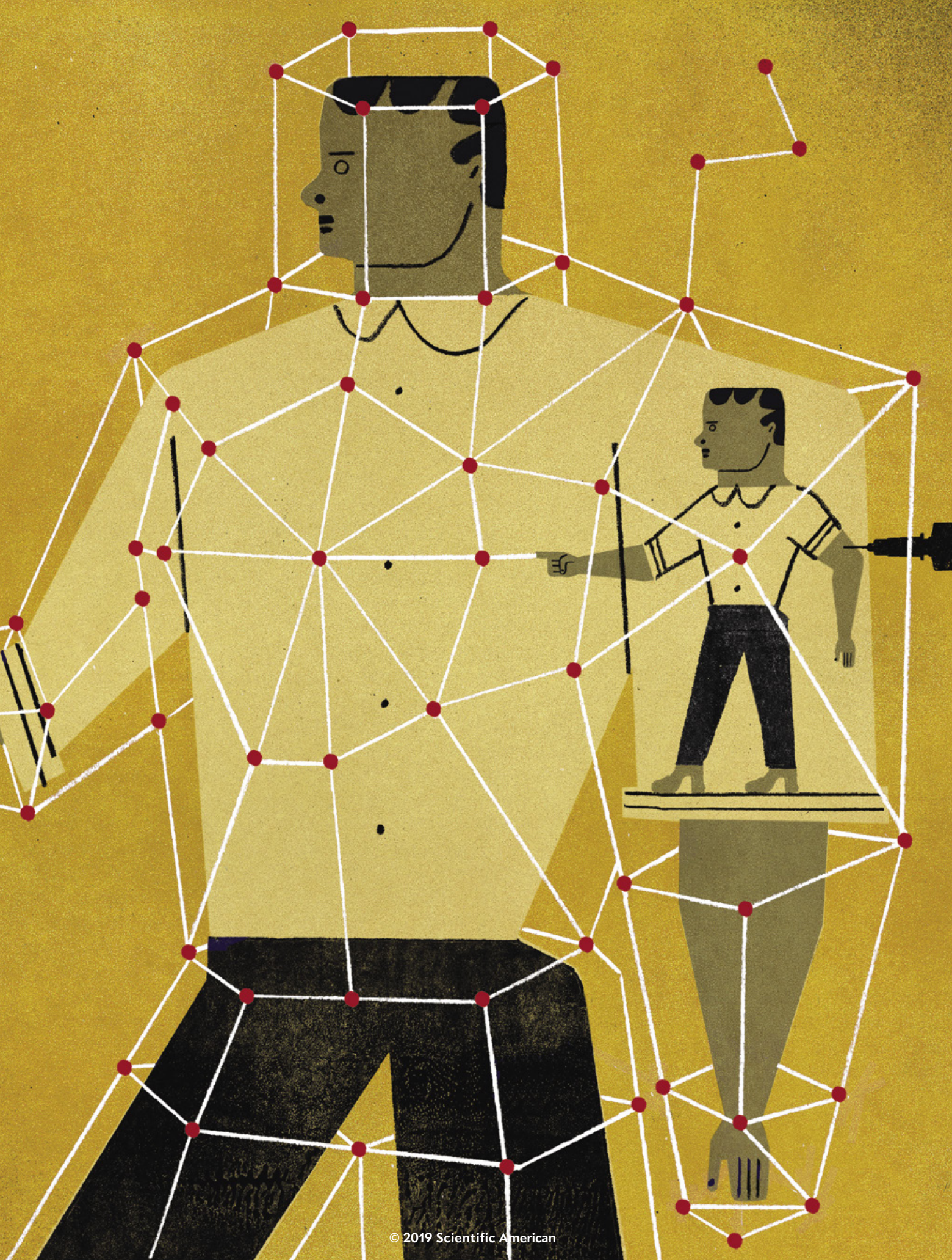
Vaccines Reimagined

A controversial theory holds that one immunization, given properly, can protect against many diseases besides its target

By Melinda Wenner Moyer

Illustration by David Plunkert





Contributing editor **Melinda Wenner Moyer** wrote "American Epidemic" (May 2018), which won second place for health policy in the Awards for Excellence in Health Care Journalism.

THE HEAT OF THE SUN, A BLAZING BASKETBALL IN THE WEST AFRICAN SKY, WAS softened by a breeze one afternoon last spring. Every so often the wind whisked a mango off a tree branch and dropped it with a thud on the corrugated iron roof that covered the health center in Bissau, the biggest city in the tiny country of Guinea-Bissau, where the rust-colored ground hadn't felt a raindrop in six months. Inside the building, the air was still and dry, and a line of women and toddlers were sticky with sweat.

An 18-month-old named Maria with thick, dark braids studied me nervously as she perched on her mother's lap. (The child's name has been changed to protect her privacy.) Next to them, Carlito Balé, a soft-spoken doctor in a short-sleeved, white button-down shirt, talked with Maria's mother in Portuguese creole, a percussive fusion of Portuguese and African dialects. Balé was telling the mother that Maria was eligible to participate in a clinical trial to test whether an extra dose of measles vaccine prevented not just the measles but many childhood infections that cause serious illness and death.

IN BRIEF

Vaccines target specific diseases, but a line of studies suggests that some offer much broader protection. **Live immunizations** in particular may cut child mortality rates by 50 percent overall, research indicates. **This work,** spearheaded by Peter Aaby and Christine Benn in Guinea-Bissau, has also drawn criticism for overstated conclusions.

In the U.S., where life-threatening infections are rare, such a trial might not garner many volunteers. But in Guinea-Bissau, where lives have been scarred by decades of scant resources and poor medical care, families lined up in droves. The nation is one of the world's poorest, and the CIA ranks infant mortality there as the fourth highest among 225 countries. Mothers often wait months to name their babies because one out of every 12 will die before his or her first birthday.

The researchers leading the trial—anthropologist Peter Aaby and physician Christine Benn, whom I had traveled to Guinea-Bissau to meet—have amassed evidence that a few specific vaccines can thwart a multitude of threatening plagues. Over decades they have published hundreds of studies suggesting that live, attenuated vaccines, which are made from weakened but living viruses or bacteria, can stave off not just their target infections but other diseases, such as respiratory infections (including pneumonia), blood infections (including sepsis) and diarrheal infections. In a 2016 review published in the journal *BMJ,* a research team commissioned by the World Health Organization analyzed 68 papers on the topic, many of which came from Aaby and Benn's research. It concluded that the measles and tuberculosis vaccines "reduce overall mortality by more than would be expected through their effects on the diseases they prevent." Some of the research the team evaluated linked the measles vaccine with a whopping 50 percent lower risk of death from any cause.

This notion that live vaccines have what are called "off-target" effects—and powerful ones—has implications that stretch far beyond Africa. In 2017 in the U.S., for instance, researchers at the Centers for Disease Control and Prevention reported that children were half as likely to be hospitalized for nonvaccine-targeted infections between the ages of 16 and 24 months if the last immunization they had received was a live vaccine rather than an inactivated one. New research in immunology suggests that live vaccines can have such wide-ranging effects because they stimulate a part of the immune system that fights a broad-based war against all outside invaders, giving the system a head start on defense. "Although we still need to know much more about the details, I now have no doubt that vaccines do have some off-target effects because of the support from many different types of evidence," says Frank Shann, a pediatrician at Royal Children's Hospital Melbourne in Australia.

Yet other scientists are far less certain. Aaby and Benn's work is, in fact, quite controversial. For one thing, most of the studies from the two Danish researchers do not prove cause-to-effect connections. "Purported effects" is how Paul Fine, an infectious disease epidemiologist at the London School of Hygiene & Tropical Medicine, describes them. Kids who get live vaccines might survive longer for reasons that have nothing to do with immunizations: the children in those groups might have been healthier to begin with. To address these concerns, Aaby and Benn are now running intervention tri-

als, such as the one Maria was being recruited for. In it, children will be matched for age and basic health, but some will have only the standard single measles shot at nine months, whereas others will get an additional dose as toddlers.

The two investigators also counter that political and pragmatic concerns drive resistance to their ideas far more than do valid scientific critiques. Aaby says that his and Benn's research is inconvenient for public policy because it indicates that live vaccines should be given last in any vaccine series, which upends current immunization schedules and could inadvertently trigger parental worries about safety. Public health scientists "don't want to hear it, and I can understand why they don't want to hear it," Aaby says. And as a result, he claims, many orthodox vaccine researchers "have clearly made me persona non grata." The 74-year-old, who is bespectacled and has a salt-and-pepper goatee, fits the part of the eccentric, obstinate and misunderstood scientist so well that he has literally become one in a novel: He inspired a character in a best-selling 2013 Danish mystery book, *The Arc of the Swallow,* who gets murdered in the first chapter.

In real life, Aaby and Benn's ideas may be reaching a tipping point. The WHO wrote in a 2014 report that nonspecific vaccine effects seem "plausible and common" and worthy of more attention. Therefore, in April 2017 the agency announced it would oversee the design of two multiyear clinical trials to further test the hypothesis, although those trials have not yet begun. The two researchers, whose professional relationship has evolved into a long-term romantic one, are pushing forward with more of their own trials, too. One of them is the study Maria's mother was considering. As I watched in the health center, she decided to enroll her daughter, so Balé picked up a large envelope containing dozens of smaller sealed envelopes and held it open toward her, telling her to pick one—a step that ensured that her daughter would be randomly allocated to either the treatment or control group. Opening her chosen envelope, Balé announced that Maria would get the extra vaccine, and her mother flashed a hopeful smile. She carried her daughter into the next room, where a nurse in a long, white-and-orange tie-dyed dress, black glasses and a kind smile waited with a needle.

CHRISTINE BENN AND PETER AABY sit in front of their house in Guinea-Bissau. Much of their research on vaccines is conducted in that country.

SOFIA BUSK HANSEN

THE MEASLES CLUE

IN 1979, soon after launching a health surveillance project in Bissau, a young Aaby watched measles kill one out of every four babies in the area. That was the year he saw his first dead body, and he saw a lot more than one.

Back then, childhood vaccines were rare in Africa. The WHO estimates that in 1980, only 6 percent of African children received the first dose of live measles vaccine, and 8 percent got the first inactivated DTP vaccine, which protects against diphtheria, tetanus and pertussis. It's not as if the vaccine was new; the combination DTP vaccine was licensed in 1949, yet 31 years later fewer than one in 12 African children ever received a dose. Indeed, only a handful of childhood vaccines were even available then in Africa. In addition to the DTP and measles vaccines, there was a live tuberculosis vaccine called bacillus Calmette-Guérin (BCG) and a live polio vaccine. In 1980 in the U.S., on the other hand, 86 percent of kids received the live measles vaccine, 98 percent were inoculated with the inactivated DTP vaccine, and 95 percent had gotten live polio vaccines. African children today receive a lot more vaccines than they used to, but they still woefully lag behind the U.S.

In 1978, a year before the historic measles outbreak began, Aaby had been sent to Guinea-Bissau by a Swedish organization to investigate malnutrition. When the epidemic swept into the city, he pulled strings to import measles vaccines and began to inoculate the local children, all the while keeping track of infection and death rates. The move was a bold one: at that time, public health authorities thought that measles vaccine campaigns in Africa were essentially a waste of money and effort. In a 1981 paper published in the *Lancet,* researchers analyzed survival data after undertaking a measles vaccine campaign in Zaire and concluded that in the future, "it may be useful to think twice before allocating already scarce resources to such a programme." Measles took the lives of the weakest children, they argued; even if the vaccine prevented the infection, the spared children would die from something else soon enough.

Aaby's experience didn't support this argument. The before-and-after numbers he saw were staggering: In 1979, the first year of the outbreak, 13 percent of local children between the ages of six months and three years died; in 1980, when the measles vaccine was available, only 5 percent did. Surprisingly, deaths from causes other than measles dropped by one fifth between 1979 and 1980, too. The trend continued. Even after measles disappeared, immunized children remained more likely than their unvaccinated peers to survive other infections. "It was one of those moments where you can suddenly see something you would never have believed

was possible," he recalls. Aaby and his colleagues wrote a letter to the *Lancet* refuting the theory that measles inoculation campaigns in Africa were useless—his first ever publication in a medical journal. After that, he says of the measles vaccine, "I became obsessed."

Aaby has now published more than 100 studies on this one vaccine. His surveillance program, the Bandim Health Project, a collaboration between Guinea-Bissau's Ministry of Health and the State Serum Institute in Denmark, is one reason why. For more than 40 years the project has been registering all pregnancies, births and deaths in Bissau's urban district of Bandim, as well as in five nearby rural regions. Aaby's team there has monitored the health of more than 500,000 people living in these areas and has collected data on hospitalizations, vaccinations and health-related choices, such as whether people sleep with mosquito nets. One day during my visit, as I walked around with Aaby, a mother holding a baby said she remembered him from when he visited her as a child some 30 years ago. His colleagues and assistants in the project affectionately call Aaby *Homem Grande,* which translates to "Big Man."

Aaby has always been a bit of a lone wolf—he spends many days working by himself in his home office—but less so during the past 15 years. While Benn was in medical school in 1992 at Aarhus University in Denmark, she was advised to reach out to Aaby because she wanted to study whether vitamin A supplementation, routinely given with the measles vaccine in developing countries, interacted in any way with the vaccine. "I still have the piece of paper with his number," Benn, who is 50, tells me as she sits on a bench in Aaby's back garden, her arms hugging her legs. She has been working with Aaby ever since. Benn is now a professor of global health at the University of Southern Denmark and runs the Danish arm of the Bandim Health Project. She is prolific, having published more than 200 papers on issues including the nonspecific effects of vaccines and the impact of vitamin A supplementation on infants in developing countries. She calls Denmark home but spends about 10 weeks a year in Guinea-Bissau. The two researchers bring to the field, and their relationship, complementary personalities: Benn, effervescent and philosophical; Aaby, serious and precise.

For the most part, Aaby and Benn's work on the measles vaccine has supported Aaby's original observations. In a landmark 1995 *BMJ* paper, they analyzed data from 12 previously published studies—some their own—on the association between measles vaccination and mortality in developing countries. They found that the vaccine was linked to a 30 to 86 percent reduction in overall death risk. In each study, measles itself only killed a small proportion of unvaccinated kids, so the vaccine wasn't just preventing measles; something else was going on. In a 2014 paper published in *JAMA,* Aaby and Benn collaborated with Danish researchers to investigate whether these protective effects extended to high-income countries. They found that Danish children who received the live measles-mumps-rubella (MMR) vaccine as their last inoculation were 14 percent less likely to be hospitalized for any infection than were kids who had most recently received the inactivated DTaP-IPV-Hib vaccine for diphtheria, tetanus, acellular pertussis, polio and *Hemophilus influenzae* type B. This study inspired the 2017 analysis by the CDC that found live vaccines to be associated with even stronger protection in the U.S.

Aaby and Benn have also linked the BCG vaccine with lower neonatal mortality, and they have studied the live oral polio vaccine (OPV) as well. In a 2018 paper, they reported that child mortality rates were 19 percent lower after OPV campaigns than before them, and a clinical trial they published in 2015 found that OPV given within two days of birth with BCG reduced mortality risk by 42 percent, compared with BCG alone. Based in part on their findings, 15 scientists wrote a letter to the *Lancet* in 2016 arguing that the global switch from live OPV to IPV, the inactivated polio vaccine, which is part of a plan developed by the international Global Polio Eradication Initiative, could inadvertently increase child mortality.

The two scientists are certain that the evidence they have accumulated points to a clear conclusion: vaccines have more profound effects on the body than we thought. The big mystery they have been grappling with is how, exactly, all this happens.

A BROAD BOOSTER

MIHAI G. NETEA MAY HAVE AN ANSWER. In 2010 Netea, an immunologist at Radboud University in the Netherlands, embarked on a study that he frankly didn't think would be all that interesting. His laboratory was studying how the BCG vaccine affects human immune cells—how it teaches them to recognize and attack the bacterium *Mycobacterium tuberculosis*. To provide an experimental control on one test, lab workers exposed blood samples from vaccinated volunteers to *Candida albicans,* a common yeast. Based on accepted immunology doctrine, which holds that vaccines incite immune responses specific to the targeted pathogen, BCG should have had no effect on the blood's response to *Candida*.

A few weeks later the student running the test approached Netea, concerned. "I think I did something wrong because I see differences with both tuberculosis and with *Candida*," Netea recalls her saying. Perhaps her samples had been contaminated; he suggested that she collect more blood samples and do the experiment over. She did, but the same thing happened. "She came again and said, 'Well, I don't know what to do, but I see precisely the same thing again,'" Netea says. He was flummoxed, so he started reading about BCG and found a handful of surprising animal studies that suggested the vaccine also protected some animals against malaria, influenza and *Listeria monocytogenes,* a common cause of foodborne illness.

That is when Netea's simple study transformed into a Greek siren, a creature beckoning for his full attention. How could a vaccine against tuberculosis change how the body responds to other pathogens? The idea contradicted established paradigms. Immunizations prime the body to make proteins called antibodies that recognize, attach to and attack proteins on the pathogens if the body ever encounters them again. This defense is called adaptive immunity, and it acts like a team of snipers that take out only certain targets. Given adaptive immunity's specificity, it didn't make sense to Netea that it could be responsible for BCG's ability to protect against a number of insults.

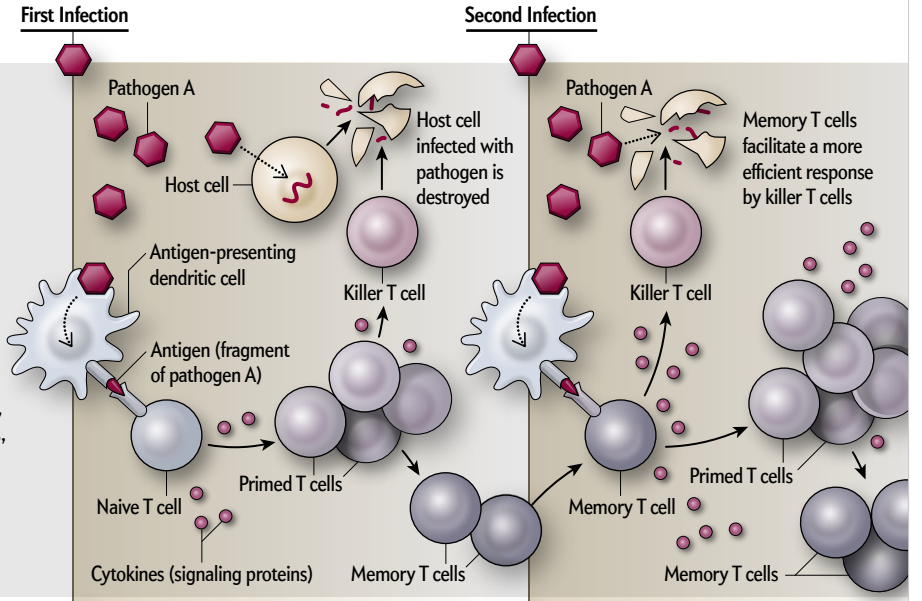
Another kind of bodily defense—one that researchers historically thought vaccines had little to do with—is known as innate immunity, and it is more like a battalion told to open fire on anyone who edges into its line of sight. It is the rapid-response team, initiating a fight against any new invader. When pathogens invade, innate inflammatory cells get pulled to the infection site. Large white blood cells called phagocytes—particularly a type called macrophages—engulf and destroy the pathogens. They also secrete immune chemicals called cytokines that draw other immune cells to the scene. The reaction creates proteins that tag pathogens so that they are easier for phagocytes to find.

Double Defenses

The body's immune system has two arms: adaptive and innate. The adaptive arm creates cells that respond only to specific bacteria or other threats. The innate arm has a faster response, but effectiveness against a particular germ is more limited. A new theory holds that this arm can be "trained" by vaccines with live but weakened pathogens to be more potent against a range of germs.

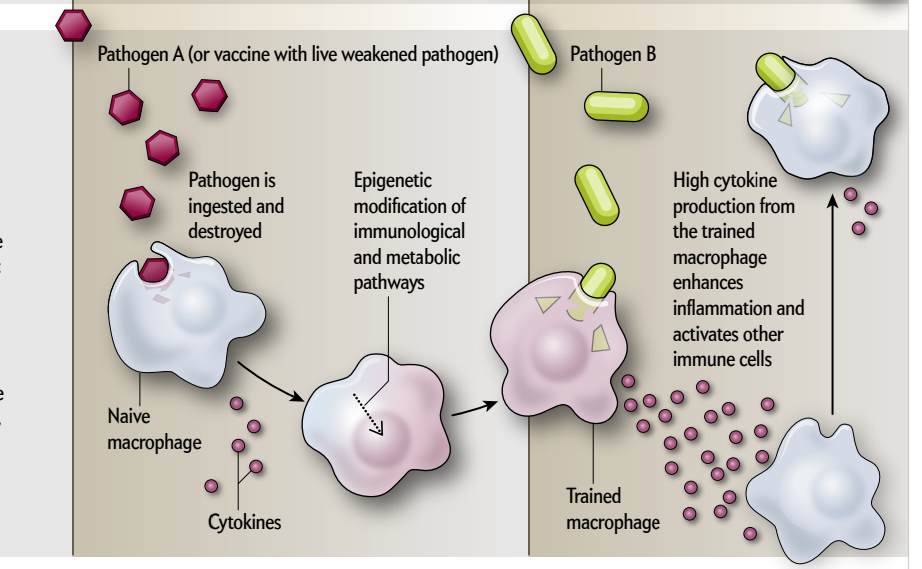
Adaptive Immunity

This part of the immune system begins by capturing pieces of an invading pathogen called antigens. Cells present the antigens—often proteins from bacteria or viruses—to T cells, transforming them from "naive" to "primed." The cells use the antigens to trigger an immune reaction specific to the invader. The response involves killer cells that go after the infected cells, chemical messengers called cytokines that activate other destructive responses and the creation of memory cells that stay in the body to recognize the pathogen, should it show up again. If reinfection happens, memory cells enable the immune system to single out the pathogen and attack it.



Innate Immunity

This arm uses general defense cells called macrophages. They engulf any pathogen and do not have specific targets. But recent research hints that innate components, like adaptive ones, can remember past pathogen encounters. Such encounters may come from a weakened pathogen in a live vaccine, and the meetings mark macrophages "epigenetically": the configuration of their DNA is changed and passed to daughter cells. These changes enhance immunological responses to several pathogens, not just one, and alter macrophages' metabolism to make them more active defenders. Should a different pathogen attack, the cells produce extra cytokines that trigger inflammation and other bodily processes that harm invaders.



SOURCES: "TRAINED IMMUNITY: A PROGRAM OF INNATE IMMUNE MEMORY IN HEALTH AND DISEASE," BY MIHAI G. NETEA ET AL., IN *SCIENCE*, VOL. 352; APRIL 22, 2016, AND "INNATE IMMUNE MEMORY: A PARADIGM SHIFT IN UNDERSTANDING HOST DEFENSE," BY MIHAI G. NETEA ET AL., IN *NATURE IMMUNOLOGY*, VOL. 16; JULY 2015

Given that BCG was increasing protection to multiple pathogens, it made sense to Netea that the innate immune system might be involved. But conventional thinking held that the innate immune system could not "remember" past immunological encounters, such as stimulation from previous vaccines. The thinking has long been that innate immune cells attack whatever they see and then forget about the battle afterward, like a soldier with amnesia. But these assumptions have been woefully incorrect.

In a paper published in 2012 in the *Proceedings of the National Academy of Sciences USA,* Netea's team found that human immune cells primed by BCG produce four times as much of a key cytokine called IFN-gamma (IFN-γ) and twice as much of the cytokines TNF and interleukin-1 beta (IL-1ß) when later exposed to other pathogens. The cells can initiate these enhanced responses for as long as three months after vaccination, which suggests that the innate immune system can, in fact, remember what it learns. More recently, in 2018, the researchers reported that BCG reprograms human immune cells in ways that help them stave off the yellow fever virus.

Netea "has really pioneered a new field within innate immu-

Illustration by Jen Christiansen

NEWBORN CHILD GETS VACCINATED against tuberculosis in a Guinea-Bissau hospital. Some studies indicate the shot protects against many diseases.

nology," says Helen Goodridge, an immunologist at Cedars-Sinai Medical Center in Los Angeles. Studies by other labs also support his theory, showing that the measles vaccine boosts the body's immune response to the toxin produced by tetanus bacteria, as well as its response when exposed to *Candida*.

It is unclear how the measles vaccine elicits its broad effects, but Netea's work suggests that BCG trains the innate immune system by initiating changes in cellular metabolism and by shaping how key immune genes are controlled. After a person gets BCG, little molecular stamps are placed on important immune-related genes, and these stamps later identify the genes so that they can be quickly turned on when another pathogen invades. Why would a live vaccine elicit these effects better than an inactivated one? Researchers theorize that live organisms may stimulate a different reaction simply because they are alive—not just bits and pieces of an organism, as in the inactivated shots. (Real full-on infections, such as measles, do not seem to produce these advantageous effects and can actually suppress immunity.)

While wrapping up his 2012 study in *PNAS,* Netea stumbled across a trial that had just been published by Aaby and Benn suggesting that BCG reduces general neonatal mortality—a finding that was criticized for being biologically impossible. Excited, Netea wrote to Aaby, telling him that he had just discovered a mechanism that made sense of his findings. Since then, the two researchers and Benn have been working together to tease out the immunology behind the Guinea-Bissau data. Vaccines seem to "change the immune system, and they don't just change it in the adaptive, pathogen-specific way," says Tobias Kollmann, an immunologist and infectious disease physician at the University of British Columbia, who sometimes collaborates with Aaby, Benn and Netea. "They change it in all kinds of different ways."

TRIALS ON TRIAL

NEAL HALSEY AGREES that Aaby has made important contributions to vaccine research over the course of his career—but his work on off-target effects is not one of them. Halsey, former director of the Johns Hopkins University's Institute for Vaccine Safety, goes back a long way with the Danish scientist. He remembers that in the 1980s, Aaby was the first to identify a potential safety problem with a new, more concentrated measles vaccine introduced in Guinea-Bissau and other developing countries. At first, no one believed him—this appears to be a recurrent Aaby pattern—but then Halsey looked at data he had collected in Haiti and saw the same effects. Based largely on their findings, the WHO withdrew the vaccine from use in 1992.

But today Halsey thinks that Aaby is putting his convictions before the science. At the 2018 World Vaccine Congress in Washington, D.C., Halsey said the data from Guinea-Bissau may be real, but Aaby and Benn have been drawing causal conclusions from it that they shouldn't. Kids who get vaccinated on time are often quite different from those who don't: they can be healthier to begin with, or they can have wealthier parents with the means to drive them to the doctor and take better care of them in general. Concluding that vaccines are responsible for broadly different medical outcomes is too much of a stretch, Halsey says.

A 2017 *BMJ* study from the Netherlands illustrates his point. Researchers analyzed hospitalization rates among toddlers who had received a live vaccine as one of their last shots and then compared them with hospitalization rates among toddlers who had most recently gotten only inactivated vaccines. Scientists found that the live-vaccinated kids were 38 percent less likely than the others to be hospitalized for infections—but those children were also 16 percent less likely to be hospitalized for injuries or poisoning. Vaccines should not affect accident risk; the fact that the researchers found this link underscores the notion that vaccine history aligns with other factors in one's life. The authors concede, though, that the way vaccines are administered in the Netherlands—they are scheduled in advance, and parents usually cancel appointments only if their kids are sick—most likely inflates the "healthy vaccinee" effect, as it is called, and findings from other countries may not be skewed so heavily.

Because it is so difficult to interpret causality from observational studies, Halsey and others have called for Aaby and Benn to conduct more randomized controlled trials, the so-called gold standard for teasing out an intervention's effects. In these studies, children are randomly selected to receive vaccines or placebos and then followed over time. This random allocation eliminates the chance that socioeconomic status or overall health will play a role in vaccine decisions. The problem is that vaccines are already recommended public policy around the world, so it is unethical

MELINDA WENNER MOYER

for researchers to deny children vaccinations to study them. Thus, scientists must get creative—they either have to design trials that provide children with extra vaccines or early ones, or they have to take advantage of natural delays in vaccine receipt.

To undertake a clinical trial in Guinea-Bissau is especially difficult. Aaby and Benn must store vaccines in a refrigerator at their house, where they have a generator, because the electrical grid is so unpredictable (they lost power every day during my visit). Political instability is another problem: one of their attempted trials was disrupted by a devastating civil war in 1998, in which Aaby also suffered a near-fatal wound when he was lanced by a piece of iron left behind by a thief who had looted his house. Some Bissau residents speak only rare dialects, which makes things difficult as well, and many don't have phones.

Despite these challenges, Aaby and Benn are trying randomized trials, such as the one involving Maria. In a few completed tests, the results have not always supported their earlier findings. In a 2018 trial that Aaby and Benn worked on, for instance, researchers found that babies who got the recommended measles vaccine at nine months, plus an additional measles shot between four and 4.5 months, were no less likely to be hospitalized or to die than babies who did not get the extra doses. Yet the two are convinced the vaccine effects are real, just not fully understood. Halsey, though, finds their dogged persistence concerning. "Very good objective scientists acknowledge when an initial observation they made is shown not to be true," he says.

Aaby and Benn are unpopular for another reason: they have published studies suggesting that inactivated vaccines, such as DTP, have detrimental effects, particularly for girls. Even though these vaccines protect against their targeted diseases, Aaby and Benn have linked these shots to a higher risk of other infectious diseases. It is unclear why this would happen—perhaps exposure to dead pathogens makes the immune system more tolerant of other future intruders—and critics argue the associations are not just spurious but also dangerous because they could further undermine the public's confidence in vaccines. "Some of them just think that I'm a madman making trouble," Aaby concedes.

A SEARCH FOR CLARITY

HIS BATTLES, HOWEVER, are entering a new phase. Although Aaby notes that his own research funds are running short, the WHO says that it will soon step into the arena. Aaby first contacted the agency about his findings in 1997; in 2013 it established a working group to review the data. In 2014 the WHO noted that the issue deserved further attention, and in 2016 and 2017 it discussed plans to oversee additional trials. One trial will investigate the effects on infant mortality of giving BCG vaccination at birth versus a placebo. The other will evaluate the effects of an extra dose of measles vaccine given with DTP between 12 and 16 months of age.

Aaby and others worry, however, that these trials will yield little clarity. The subjects will be given inactivated vaccines either at the same time as the live vaccines or after them, which, according to Aaby's previous findings, could mute potentially beneficial effects. "We discussed this at length with many experts, and the evidence is clear that those trials will not give the answer," Kollmann says. Shann, the Australian pediatrician, agrees. These trials will be "a scandalous waste of time and money," he says, because "none of those involved really understands the field." And right now it is unclear when the trials will start. WHO spokesperson Tarik Jasarevic says that as of early 2019, the agency has not found financial sponsors for the work.

Ultimately Aaby worries that the WHO is just going through the motions. He suspects the agency wants to appear that it is doing due diligence after its 2014 report on nontargeted effects but that its real goal is to make the issue go away. If nonspecific effects are real and powerful enough to save lives, then public health agencies will have to consider making changes to the vaccine schedule and perhaps even replace some inactivated vaccines with live ones, which would be extremely difficult.

Last year I asked Frank DeStefano, director of the CDC's Immunization Safety Office, what it would take to make such changes in the U.S. "Certainly evidence would have to be stronger that this is a real effect," he said. He noted that the agency had no plans at that time to collect more data on the issue. But even if it had additional evidence, he said, the CDC would have to consider all the possible risks and benefits before making policy changes.

The evening I left Guinea-Bissau I sat in the back garden with Benn, eating Danish cheese that she brought with her from her last trip home, and I thought about the couple's philosophy of science. These researchers are not shy about their beliefs; they are convinced that nonspecific effects are real but so complex that many details remain a mystery, and they are not afraid to say so. To critics, this strength of conviction is a great weakness, a blazing preconception that biases their results. And it may do so. But bias is not unique to them. Scientists are people—people with ideas, and prejudices, and feelings—and every study involves interpretation. How do we know whose interpretations edge closest to the truth? Are those who admit to their beliefs more biased than those who don't? Who should decide when enough evidence has amassed to reach a consensus, particularly when the implications are unexpected, inconvenient and consequential? Within this small and contentious field, at least, there are no clear answers.

"You have this feeling you are pulling a thread, and you don't know how big the ball of yarn is," Benn said to me. She was referring to the research on vaccines, but she could have been speaking about the scientific process itself. Biology is immensely complicated because our bodies are complex. The practice of science is complicated, too, because it is a product of humanity—an endeavor created and shaped by our imperfect minds. If vaccines do what Aaby and Benn think they do—and that is still an open question—it will take a lot more messy unraveling before the world sees things their way. SA

MORE TO EXPLORE

Vaccine Programmes Must Consider Their Effect on General Resistance. Peter Aaby et al. in *BMJ*, Vol. 344, Article No. e3769. Published online June 14, 2012.

The Introduction of Diphtheria-Tetanus-Pertussis and Oral Polio Vaccine among Young Infants in an Urban African Community: A Natural Experiment. Søren Wengel Mogensen et al. in *EBiomedicine*, Vol. 17, pages 192–198; March 2017.

Trained Immunity: An Ancient Way of Remembering. Mihai G. Netea and Jos W. M. van der Meer in *Cell Host & Microbe*, Vol. 21, No. 3, pages 297–300; March 8, 2017.

BCG Vaccination Protects against Experimental Viral Infection in Humans through the Induction of Cytokines Associated with Trained Immunity. Rob J. W. Arts et al. in *Cell Host & Microbe*, Vol. 23, No. 1, pages 89–100; January 10, 2018.

FROM OUR ARCHIVES

Straight Talk about Vaccination. Matthew F. Daley and Jason M. Glanz; The Science of Health, September 2011.

scientificamerican.com/magazine/sa

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David Wright is co-director of the Global Security Program and is an expert on technical aspects of nuclear weapons policy.

SECURITY

BROKEN SHIELD

Missiles designed to destroy incoming nuclear warheads fail frequently in tests and could increase global risk of mass destruction

By Laura Grego and David Wright

Illustrations by Tavis Coburn

EARLIER THIS YEAR IN A HIGH-STAKES SUMMIT MEETING, THE LEADER OF NORTH KOREA, KIM JONG-UN, AND U.S. president Donald Trump failed to agree on a way to end North Korea's missile and nuclear weapons program. Within days of the summit, satellite imagery showed that Kim was rebuilding some of North Korea's rocket facilities.

In 2017 Kim's government had tested its first long-range missiles and soon followed up with a test of what appeared to be a powerful hydrogen bomb. After those operations, Trump told Americans not to worry. "We build the greatest military equipment in the world," he said on the Fox News television channel. "We have missiles that can knock out a missile in the air 97 percent of the time. If you send two of them, they are going to get knocked down."

The president was expressing extraordinary faith in the Ground-based Midcourse Defense (GMD) system, currently the country's sole guard against intercontinental ballistic missiles that carry nuclear warheads. But his faith was woefully misplaced, and facts belie his claim. U.S. military testing data show there is no basis to expect GMD interceptors to work more than about 50 percent of the time. Using multiple interceptors against each target could in some cases improve these odds but will not fundamentally change the situation. The chances of a nuclear weapon getting through in a real-world attack using multiple missiles is still dangerously high. Our analysis of all 19 tests done—the most recent one was in late March—as well as several government reviews of the program, shows an alarmingly high failure rate.

The problems with these interceptors can be traced back decades, to the beginnings of the program, because the Pentagon rushed to develop it and abandoned tried-and-true oversight and testing requirements that have been used for most major weapons. Plus, the system is vulnerable to defense-penetrating countermeasures that any country capable of building a long-range missile could take. Yet the Pentagon is moving to expand the troubled interceptor fleet despite already spending more than $40 billion to produce these unreliable results.

THE ARMS RACE

THE WORLD has been living under the threat of nuclear-armed intercontinental ballistic missiles (ICBMs) since the late 1950s. Two nuclear-armed nations, the former Soviet Union and the U.S., were desperate to deter each other from using these weapons. Both built more missiles, armed with multiple warheads, to overwhelm any response the other country might be able to mount. This cycle of action and reaction resulted in the rapidly growing potential for mass destruction.

Eventually U.S. and Soviet leaders recognized the dangers of this tit for tat, and in 1972 they signed the first Strategic Arms Limitation Treaty (SALT I). They also agreed to the Anti-Ballistic Missile (ABM) Treaty, which strictly limited defenses against long-range missiles and served to break the cycle of defensive advances prompting the other side to improve its offense. These arms-control agreements and those that followed did the job. The break-neck growth of the U.S. and Soviet nuclear arsenals peaked in 1986 at more than 60,000 weapons, and three decades of arms reductions have brought that number down to fewer than 10,000 today.

While the stockpiles were still high, in 1983, President Ronald Reagan—driven by distrust of the Soviets and faith in new technologies—tried to revitalize missile defense and announced the Strategic Defense Initiative, or "Star Wars." His vision was based on nonexistent and impractical innovations, such as space-based lasers powered by nuclear explosions, and after a while plans for the system were scrapped.

But research on strategic missile defense technology continued as new threats emerged. North Korea's pursuit of nuclear weapons and ballistic missiles, which became apparent in the 1990s, provided a fresh argument for strategic defenses that took advantage of improvements in missile tracking and interceptor guidance. Still, limitations of the technology, skepticism about the magnitude of the threat, and concerns that deploying defenses would threaten the successful and ongoing arms-reduction process led the Clinton administration to respect the ABM Treaty limits.

Then, on September 11, 2001, everything changed. In the political environment following the attacks on the World Trade Center in New York City and the start of the "war on terror," opponents of missile defense found it difficult to argue against any military programs. Congress could muster only limited debate on arms control. In late 2001, citing a potentially growing threat from rogue nations and terrorism, the George W. Bush administration announced that the U.S. would withdraw from the ABM Treaty. Then the government said it would rush ahead with a plan to build a missile defense system. The era of negotiated limits on missile defenses was over.

THE INCOMING THREAT

DESTROYING an ICBM's warhead is not easy. These missiles launch thousands of kilometers from their targets, accelerated by powerful engines in what is called their boost phase. Within minutes they reach speeds of about 25,000 kilometers per hour and then can release multiple warheads that arc through the vacuum of space. After about half an hour of this midcourse flight, they re-

IN BRIEF

For more than a decade the U.S. has been testing a system to intercept incoming nuclear missiles. It shows alarming unreliability and vulnerability.

Problems stem from a rush to deploy the system, called the Ground-based Midcourse Defense, and abandonment of standard quality controls.

These interceptor missiles have already been put in the field and greatly add to global nuclear risks while offering minimal protection.

THE TROUBLED PAST OF MISSILE DEFENSE

The U.S. has struggled to make effective long-range missile interceptors, including the Ground-based Midcourse Defense system, and diplomatic approaches have often been undercut.

MARCH 23, 1983

President Ronald Reagan announces the nation will start an expanded R&D program for missile defense, called the Strategic Defense Initiative, or SDI.

1980

1990

MAY 1972

U.S. and Soviet Union sign the Anti-Ballistic Missile Treaty, limiting defense technology.

JANUARY 29, 1991

In place of the SDI, President George H. W. Bush announces the Global Protection Against Limited Strikes (GPALS) system to counter unauthorized, accidental or limited attacks.

JULY 31, 1991

Presidents Bush and Mikhail Gorbachev of the former Soviet Union sign START I, reducing arsenals to 6,000 deployed warheads on each side.

Ground-based Midcourse Defense (GMD) System Tests

◆ Success ◆ Failure

enter the atmosphere and drop toward their targets in the terminal flight phase, which lasts only a few minutes.

Defense efforts have focused on the midcourse period because it lasts much longer than the boost phase, and by intercepting at long distances from the targets, the system can defend much larger areas than it could at the terminal stage. The earliest interceptors carried their own nuclear weapons to blow up the incoming warhead. But in the late 1970s development began on prototype interceptors that carried a nonexplosive "kill vehicle." Onboard sensors were supposed to guide the vehicle into the incoming warhead during its midcourse phase. At a collision speed of 10 kilometers per second, the kinetic energy per mass is more than 10 times the energy released by a similar amount of high explosives, so such impacts could destroy warheads in a direct hit and avoid the use of a nuclear detonation for defense. This "hit to kill" method requires sophisticated technology. The kill vehicles must be guided to within centimeters of a precise target point on the incoming missile warhead.

Bush's plan was to get a system into the field quickly and then improve it. In September 2004 the administration stated that the system had achieved a "limited deployment option," which meant it could be turned on and used if necessary. Only five interceptors were in place the day of that announcement.

Today the GMD comprises space-based sensors, terrestrial radars, 44 interceptors based in Alaska and California, and facilities and personnel to control operations. The Department of Defense's current plan is to increase the number of interceptors to 64 by 2023 and possibly add more soon thereafter to reach a total of 100.

HOLES IN THE DEFENSE

THE PUSH TO DEPLOY this system, however, has produced serious shortcomings, and the GMD has yet to demonstrate a useful military capability. The roots of the problems lie both in the shortcuts the government took to move the program forward and in the technical complexity of missile defense.

In 2002 Bush's DOD exempted the program from the Pentagon's traditional "fly before you buy" oversight rules, intended to make sure major defense systems and equipment work well before the nation has to depend on them. Under those rules, the GMD system would need to meet criteria for technical maturity and effectiveness and to undergo demanding operational tests to ensure that it worked as required under real-world conditions before being put in the field. But Bush's exemption meant that prototype interceptors for research and development—by definition not intended for the real world—could be used in urgent situations. While faster, this approach permits the use of unreliable or poorly tested equipment.

In 2014—10 years after the limited deployment announcement—all GMD interceptors in the field were put there before the Pentagon had conducted a single successful intercept test of their design, according to reviews by the DOD and Congress. Ideally, a rigorous engineering process identifies problems early and allows them to be fixed before deployment. But with the GMD system, failed intercept tests revealed design flaws that required expensive retrofits of dozens of interceptors already in silos. Because the interceptors were being fielded as they were being tested, hardware and software components and designs vary from interceptor to interceptor, making it difficult to use the performance of one to predict that of another or to resolve problems across the entire fleet.

GMD interceptors have destroyed their targets in just more than half the 19 intercept tests conducted. The record is not improving with time. Six of the 11 tests since 2004 have failed to destroy their target. Of the most recent six tests, three have failed.

PENELOPE BREESE *Getty Images*

AUGUST 31, 1998

North Korea launches a Taepodong-1 missile over Japan, but the third stage fails to put its payload in orbit.

MAY 24, 2002

Presidents George W. Bush and Vladimir Putin of Russia sign the Strategic Offensive Reductions Treaty (SORT), limiting the two sides to between 1,700 and 2,200 operationally deployed warheads each.

JUNE 13, 2002

U.S. officially withdraws from the ABM Treaty.

DECEMBER 2016

Congress scraps the 1999 Missile Defense Act language; removes the word "limited" from the missile defense mandate.

2000

2010

JANUARY 3, 1993

Presidents Bush and Boris Yeltsin of Russia sign START II, limiting deployed warheads on each side to 3,000 to 3,500.

OCTOBER 2, 1999

First successful intercept test of prototype GMD warhead kill vehicle.

JULY 22, 2004

First GMD interceptor installed in silo at Fort Greely, Alaska.

SEPTEMBER 30, 2004

The U.S. government declares that the GMD system is capable of a limited deployment option.

JULY 4, 2017

First test of North Korean missile with apparent intercontinental range.

*INTERCEPTOR FAILED TO DESTROY TARGET, ALTHOUGH MISSILE DEFENSE AGENCY LISTS TEST AS SUCCESS.

A number of these failures were attributed to lapses in quality control, according to the Missile Defense Agency, the Pentagon office that runs the program. The agency stated in 2007 that poor manufacturing and setup procedures by its contractors—which it attributed to the streamlining of the acquisition process and schedule pressures—had caused "test failures and slowed production." A failed $236-million intercept test in January 2010 was attributed in part to a small device called a lockwire, which Raytheon, the contractor that builds the kill vehicles, did not install. A report by the DOD's inspector general, following that mistake, found many other serious quality-management problems.

These quality-control troubles can slow progress by masking other flaws that tests are supposed to uncover. For example, the January 2010 test was repeated later that year and failed again, but that time the trouble was attributed to a design flaw: vibrations from the rocket motors the kill vehicle uses to change direction could cause errors in the guidance system. This design issue might have been identified earlier if the missing lockwire had not derailed the earlier test. Identifying the bigger problem and fixing the interceptors that had already been put in the field eventually cost nearly $2 billion.

Another disturbing aspect of the high failure rate is that it has occurred in highly simplified tests that do not resemble situations an interceptor would face against an actual enemy. No GMD test, for instance, has involved an incoming missile that used countermeasures such as realistic decoys. Incoming weapons can carry numerous decoys that appear very similar to warheads; the GMD must find the real warhead among the fakes. But tests have deliberately used decoys that appear very different from the actual mock warhead, making the interceptor's job artificially easy.

"If we can't discriminate what the real threatening objects are, it doesn't matter how many [ground-based interceptors] we have. We won't be able to hit what needs to be hit," Michael Gilmore, then director of Operational Test and Evaluation for the Pentagon, told Congress in 2013.

The poor test record of the GMD system stands in stark contrast to repeated statements by U.S. military and political officials over the years that give an inaccurately optimistic appraisal of the system. For example, in congressional testimony in April 2016, Admiral Bill Gortney, then commander of the North American Aerospace Defense Command and U.S. Northern Command, said, "We are prepared to engage and protect Hawaii, Alaska and all the rest of the states with the existing system and have high confidence in its success." In fact, the system has not demonstrated capability under real-world conditions. The most recent test, in March, was the first one that the Pentagon actually described as operational rather than developmental. The agency said the interceptors (it fired two) destroyed the target, but it has not released enough information about the test to permit an independent evaluation of the test conditions.

INEFFECTIVE DETERRENCE

EVEN WHILE ACKNOWLEDGING the GMD's limits, some contend that any capability is better than none. This argument, however, has serious flaws.

The 2019 *Missile Defense Review* asserts that a missile defense system such as the GMD helps to deter a missile attack by increasing an adversary's uncertainty. The attacker might doubt its ability to destroy enough U.S. forces to avoid a retaliatory strike, for instance. But such doubts are already in place: U.S. retaliation is assured by nuclear forces safely hidden on subma-

DAVID AKE *Getty Images (George H. W. Bush and Boris Yeltsin);* KONSTANTIN ZAVRAZHIN *Getty Images (George W. Bush and Vladimir Putin);* U.S. MISSILE DEFENSE AGENCY *(interceptor);* GETTY IMAGES *(Kim Jong-un)*

rines at sea. And this logic certainly does not apply to an adversary whose intent is not to target U.S. retaliatory capability in the first place, such as North Korea or even China. Those nations' missile arsenals are too small and inaccurate to mount an effective strike against U.S. nuclear forces. Instead they would target cities or other large, unprotected sites. Therefore, missile defense is unlikely to offer anything that adds to the deterrence currently provided by U.S. forces.

The *Missile Defense Review* also argues that the U.S. needs a defensive shield so an adversary's missile threats cannot force this nation away from taking military actions in its own interests or on behalf of an ally. But to make U.S. decision makers confident enough to ignore adversarial threats, a system such as the GMD needs to demonstrate high effectiveness, and it has not.

At its core, missile defense is meant to defeat a nuclear attack if deterrence were to fail. While this is where the "some is better than none" argument is the most persuasive, for any realistic scenario, missile defense will likely do very little. Even if the system's ability to deal with real-world complexities such as countermeasures were greatly improved, a nuclear attack will still present enormous risks. For example, if the system achieved an improbably high 95 percent effectiveness against one missile, in an attack by just five missiles there is still a one-in-four chance of at least one nuclear warhead penetrating the defense. The likelihood of a city being destroyed would be higher than correctly predicting the roll of a die. The effectiveness against a real attack is likely to be much lower.

What missile defenses may actually do is get in the way of reducing the nuclear threat faced by the U.S. or even increase it. As long as nations such as Russia and China continue to rely on strategic arsenals for deterrence, pursuing defenses that appear to threaten that deterrent—or that lay the groundwork for a system that may threaten it in the future—will at best hinder nuclear reductions. At worst these efforts will lead to the growth of more offensive weapons designed to overwhelm the defense and reduce stability by increasing the incentive to launch missiles first in a crisis.

There is growing evidence that global powers are already returning to this type of brinkmanship, which the ABM Treaty sought to quell. As part of its ratification process for the 2011 New START arms-control treaty with the U.S., Russia stipulated that further cuts to its arsenal would require limitations on strategic defenses. More recently, President Vladimir Putin announced that Russia is developing several new strategic nuclear delivery systems that are designed specifically to defeat or evade U.S. missile defense systems. These include a nuclear-capable hypersonic weapon that could fly undetected by current sensors and a drone submarine that could carry nuclear weapons designed to destroy U.S. coastal cities.

China, for its part, recently added multiple nuclear warheads to its large ballistic missiles—a change the DOD, in its report to Congress on China's military power, attributed in part to concerns about advances in U.S. strategic defenses.

Beyond the potential for missile defense to increase nuclear threats the U.S. faces is the real possibility that a false sense of security will distort U.S. decision-making. Misunderstanding the system's capability and believing that missile defense is highly effective or even somewhat effective could lead U.S. leaders to take more risks in foreign policy. An unfounded faith in missile defense reduces incentives to pursue political solutions to national security problems and to improve nuclear arms control. Nuclear-armed missiles are a political problem that technology cannot solve.

HEIGHTENED RISK

ALTHOUGH THE MODEST SIZE of the current GMD system somewhat limits its destabilizing potential, missile defense proponents are pushing to expand other U.S. missile defense capabilities. The navy's Aegis ship-based missile defense system was developed to defend against short- and medium-range missiles in particular regions, but Congress has called for testing a new Aegis interceptor against an intercontinental-range missile, thus demonstrating its potential for strategic missile defense. Current plans call for deploying several hundred of these new interceptors on ships over the next two decades to establish a large, mobile, strategic missile defense capability that could be used around the world. Such a system is certain to cause concerns in Russia and China and is the kind of system the ABM Treaty was intended to stop.

The current defense budget also requests money to begin developing a space-based missile defense system designed to intercept long-range missiles right after launch, during their boost phase and before they can deploy countermeasures. These space-based systems would be enormously expensive yet vulnerable to attack and therefore ineffective—and highly destabilizing.

As with the decision to proceed with the GMD program, this missile defense expansion is taking place with very limited discussion and not enough assessment of the benefits and costs. The price is high. The total GMD cost is projected to reach at least $67 billion if the Pentagon fields 64 interceptors, according to a 2018 U.S. Government Accountability Office report. An "austere" space-based interceptor capability would require 650 satellites and cost upward of $300 billion, says a 2012 National Research Council report. Real resources are being spent on the illusion of a defense.

But there is another, even more important cost: our national security. Current U.S. missile defense plans are being driven largely by technology, politics and fear. As in the past, this is happening with insufficient understanding and consideration of the limited protection these systems can realistically provide. Missile defenses will not allow us to escape our vulnerability to nuclear weapons. Instead large-scale deployments will create barriers to taking real steps toward reducing nuclear risks—by blocking further cuts in nuclear arsenals and potentially spurring new deployments. This process of moving blindly and quickly ahead threatens to lead to a world filled with greater threats, not lesser ones. SA

MORE TO EXPLORE

2015 Assessment of the Ballistic Missile Defense System (BMDS). Director, Operational Test and Evaluation. Department of Defense, April 2016. https://apps.dtic.mil/dtic/tr/fulltext/u2/1011964.pdf

Shielded from Oversight: The Disastrous US Approach to Strategic Missile Defense. Laura Grego, George N. Lewis and David Wright. Union of Concerned Scientists, July 2016. www.ucsusa.org/nuclear-weapons/us-missile-defense/shielded-from-oversight

The Warfighter and Decision Makers Would Benefit from Better Communication about the System's Capabilities and Limitations. U.S. Government Accountability Office, May 30, 2018. www.gao.gov/products/GAO-18-324

FROM OUR ARCHIVES

The Dynamics of the Arms Race. George W. Rathjens; April 1969.

scientificamerican.com/magazine/sa

BIOTECHNOLOGY

ALL THE WORLD'S DATA COULD FIT IN AN EGG

How DNA is used to store—and generate—information at extreme scales

By James E. Dahlman

IN BRIEF

DNA has many properties that make it ideal for storing information—and not just genetic code. But it is not yet capable of replacing traditional electronic storage such as hard drives.

As sequencing methods have improved, however, researchers in fields such as chemical engineering are using DNA as a molecular recorder that allows them to generate data at unprecedented speeds.

In this way, DNA is being used to both "read" and "write" information. This progress could have big implications for accelerating drug development and treating diseases.

Photograph by Dan Saelinger

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BILLIONS OF YEARS BEFORE HUMANS DEVELOPED HARD DRIVES, evolution chose DNA to store its most precious information: the genetic code. Over time DNA became so proficient at this task that every known life-form on earth uses it. With recent technological breakthroughs that allow us to easily "read" and "write" DNA, scientists are now repurposing this age-old molecule to store new types of information—the kind that humans are generating at an exponential rate in the age of big data.

The concept of repurposing DNA to store information beyond genetic code has been discussed extensively. After all, the 1s and 0s of computer code are bumping up against the limits of physics. One of the challenges to safely storing all the data we create was exposed recently, when Myspace—once the most popular social network—announced that a decade's worth of data may have been irreparably lost in a server-migration project. The long-term protection of data, like those of a Web site that rebooted after a period of dormancy, exposes where existing technologies are vulnerable and clunky. And it's not just a spatial problem: significant energy is needed to maintain data storage.

The properties of DNA have the potential to get around these issues. For one thing, DNA's double-helix structure is perfectly suited for information storage because knowing the sequence of one strand automatically tells you the sequence of the other strand. DNA is also stable for extended periods, which means the integrity and accuracy of information can be maintained. For example, in 2017 scientists analyzed DNA isolated from human remains that were 8,100 years old. These remains were not even stored in ideal conditions the entire time. If kept in a cool, dry environment, DNA can almost certainly last tens of thousands of years. DNA is also stable for long stretches, which means the integrity and accuracy of information can be maintained.

Perhaps the most compelling aspect of the double helix, however, is that it can fold into an extraordinarily dense structure. For comparison, every individual human cell contains a nucleus with a diameter of approximately 0.00001 meter. Yet if the DNA inside a single nucleus was stretched out, it would reach two meters. Put another way, if the DNA in a person was strung together, it would extend 100 trillion meters. In 2014 scientists calculated that it is theoretically possible to store 455 exabytes of data in a single gram of DNA. This information-storage density is about a million-fold higher than the physical storage density in hard drives.

Although DNA has commonly been thought of as a storage medium, there are still significant scientific, economic and ethical hurdles to overcome before it might replace traditional hard drives. In the meantime, DNA is becoming more widely—and immediately—useful as a broader form of information technology. DNA has been used, for instance, to record old Hollywood films, preserving the classics in genetic code instead of fragile microfilm. Even more recently, DNA has been used as a tool to design safer gene therapies, speed up anticancer drug development and even generate what is perhaps the first genetic "live stream" of a living organism. On the frontiers of this evolving field, DNA is being pursued not just for long-term data storage but for facilitation of data generation at unprecedented speed. That is because DNA is more scalable than any other molecule in both directions: it allows us to dramatically expand the amount of data we create and shrink the resources needed to store them.

ACCELERATING NEW NANOPARTICLES

IN RECENT YEARS scientists have increasingly used DNA as a molecular recorder to understand and keep track of their experimental results. In many cases, this process involves DNA bar coding: To label and track the result of an individual experiment, scientists use a known DNA sequence to serve as a molecular tag. For example, one experimental outcome might be associated with the DNA sequence ACTATC, whereas another outcome might be associated with a TCTGAT, and so on.

DNA bar coding has been around since the early 1990s, when Richard Lerner and the late Sydney Brenner, both then at the Scripps Research Institute, proposed it as a way to track chemical reactions. Their concept was tremendously innovative but ahead of its time: technologies that easily and inexpensively read out DNA had not yet been developed. Its potential was only realized after many scientists made contributions to nucleotide chemistry, microfluidics and other approaches, which together enabled the advent of what is called next-generation sequencing. A major breakthrough came in 2005, when researchers reported that 25 million DNA bases were analyzed in a four-hour experiment.

Next-generation sequencing has continued to rapidly improve; it is now easy to read millions of DNA sequences at the same time, which means that thousands of experiments can be performed and analyzed simultaneously. Analyzing DNA bar code experiments with next-generation sequencing is its own form of data management: instead of testing ideas one at a time, scientists can make 20,000 predictions and test them all to see which is correct.

Biologists were the first to utilize DNA bar coding extensively. As it has become more accessible, researchers in many different fields, including chemical engineering and materials science, are using the technology to perform experiments at entirely new scales. In my laboratory at the Georgia Institute of Technology, for instance, engineers are using DNA bar codes to improve the design and function of nanoparticles so that they can safely deliver drugs to diseased cells. Nanotechnology, which relies primarily on physics and chemical engineering, may seem completely unrelated to DNA. But when you think of DNA as a way to track and store any data, its utility as an organizational tool becomes apparent.

One fundamental problem for nanotechnologists is that designing experiments to search for effective therapies is still far easier than performing them and analyzing the results. That is because the shape, size, charge, chemical composition and many other variables of individual nanoparticles can alter how well they deliver their genetic drugs to diseased cells. Additionally, these factors all interact with one another, making it a struggle for researchers to predict which nanoparticle will deliver its drug in the most targeted way. An obvious solution is to evaluate every nanoparticle one by one. But data from established pharmaceutical companies that have developed nanoparticles for RNA drugs have demonstrated that this type of testing can require several hundred million dollars to pull off.

That is where the storage capabilities of DNA can make big strides. To increase the number of nanoparticles we are able to test, we can design thousands of them with diverse chemical structures—large, positively charged spheres or small, neutrally charged triangles, for example—and assign each a DNA bar code.

Nanoparticle one, with chemical structure one, carries DNA bar code one. Nanoparticle two, with chemical structure two, carries DNA bar code two. We repeat this bar-coding process many times, thereby creating many different nanoparticles, each with its own unique molecular DNA tag. We can then administer hundreds of these nanoparticles to diseased cells. To identify the nanoparticle that most successfully delivered the drug, we use DNA sequencing to quantify the bar codes inside the cells.

The scale of such experiments is entirely new to nanomedicine. A "traditional" experiment in my field generates between one and five data points. By the end of 2019 my lab hopes to quantify how 500 different nanoparticles deliver gene therapies to 40 different cell types. Doing so is equivalent to running 20,000 experiments simultaneously.

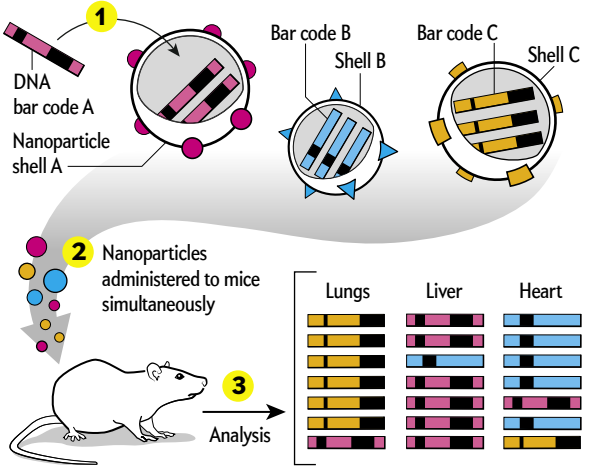
As a result, we also needed to create a data-analysis pipeline capable of monitoring data quality, as well as helping us statistically test our results. First, we measured how well results from one replicated experiment predicted delivery in another. Once we knew the large data sets were reliable, we used statistics to ask whether certain nanoparticle traits—such as their size—affected delivery to target tissues. We found that the chemistry of the nanoparticle, not its size, dictated nanoparticle delivery. Using this approach, we hope to discover safe gene therapies more quickly, using far fewer resources. One of our goals is to identify a nanoparticle that can specifically deliver gene therapies that help kill tumors, thereby reducing side effects such as nausea and hair loss that accompany existing treatments.

We have already had some success. In 2018, by using very large data sets generated by DNA bar-coding experiments, we rapidly identified new nanoparticles that deliver gene therapies to endothelial cells, which line blood vessels, as well as several types of immune cells, which govern how our bodies respond to disease. This finding could change treatment by allowing us to change the activity of proteins in immune cells that are currently "undruggable," meaning the proteins are hard to target with small-molecule drugs or antibodies. As a result of data published in journals that included the *Proceedings of the National Academy of Sciences USA, Advanced Materials* and the *Journal of the American Chemical Society* in 2018 and 2019, we received a flood of interest from other gene therapists and were able to start GuideRx, a bar-coding company that focuses on efficiently developing safe gene therapies.

DNA bar coding has now become so commonplace that it is being applied in different ways even within a single field. One ex-

Tracking Nanoparticles with DNA Bar Codes

DNA bar codes allow researchers to efficiently test nanoparticles designed for drug delivery. Previously the process was laborious and time-consuming; now hundreds of different particle types can be tested all at once. During the testing phase, as shown here, a unique DNA bar code is placed within each of the nanoparticle shell types **1**. Ultimately those nanoparticles will carry therapeutic drugs to diseased cells. Many nanoparticles are administered simultaneously for experimental testing **2**. Cells are then scanned for the DNA bar codes to see which nanoparticles gain entry to which organ tissues **3**, helping to rapidly establish which nanoparticle designs might be best suited for different drug-delivery goals while minimizing negative side effects.



SOURCE: "A DIRECT COMPARISON OF IN VITRO AND IN VIVO NUCLEIC ACID DELIVERY MEDIATED BY HUNDREDS OF NANOPARTICLES REVEALS A WEAK CORRELATION." BY KALINA PAUNOVSKA ET AL., IN *NANO LETTERS*, VOL. 18, NO. 3; MARCH 14, 2018

Illustration by Jen Christiansen

ample is cancer biology, which looks at how genetic mutations cause cancer and how new drugs can treat it. Drug resistance remains a major challenge in this field: patients often initially respond to a drug but relapse as it loses the ability to kill tumor cells.

Scientists in the lab of Todd Golub at Harvard University have used DNA bar coding to study such resistance. In 2016 they described how they used a virus to permanently insert a DNA bar code directly into the genome of cancer cells. Cancer cell type A received bar code sequence A; cancer cell type B received bar code B, and so on. The scientists mixed the different cells together, plated them on a dish and treated them with a cancer drug.

If the drug killed the cancer cell or slowed its growth, then the cell would not divide. But if the cell became resistant to the drug, then it divided rapidly. Thus, over time the relative amount of bar code sequence A increased if cell type A became resistant to the drug or, alternatively, decreased if cell type A was killed by the drug. By sequencing all the bar codes from surviving cells over time, the lab quantified how well all the cell types responded to the drug simultaneously.

Later that year the lab of Monte Winslow at Stanford University used DNA-bar-coded pancreatic cell lines to identify drugs that prevented the spread of cancer, or metastasis. The lab bar coded each cell line using a virus, then plated each cell line in its own well. Each well was then treated with an anticancer drug. In this way, drug one became associated with bar code one. Immediately thereafter, the scientists injected the cells into the bloodstream, and they later measured which cells spread to the lungs. By identifying the bar codes that were abundant or absent, the researchers identified drugs that respectively promoted or prevented metastasis.

In a third example, scientists at the Broad Institute of the Massachusetts Institute of Technology and Harvard University used DNA bar coding to study how all the genes in the genome affect a single cancer. The researchers first grew a very large number of cells and plated them in a large dish together. Then they used a gene-editing system to inactivate or, alternatively, activate all the genes in the genome one by one. The sequence of the gene whose expression had been modulated acted as the bar code. By treating the cells with a cancer drug and sequencing the DNA over time, the scientists could understand how every gene in the genome affects drug resistance.

In these approaches, DNA is acting both as a data-generating molecule, because it is required to perform all the experiments simultaneously, and as a data-storage molecule, because next-generation sequencing is used to analyze the DNA bar codes. The implications are stunning: the same techniques can be applied to autoimmune and neurological diseases and cardiovascular dysfunction. The full power of using DNA bar coding can be understood with a simple exercise. In the examples discussed earlier, replace the word "cancer" with a different disease or the word "resistance" with any desired drug response. In this way, DNA bar coding is positioned to fundamentally streamline early-stage drug development, thereby accelerating the path to effective therapies.

READING VS. WRITING

DNA BAR CODING relies on "reading" known DNA sequences. Until recently, however, it was not practically possible to "write" DNA sequences. Broadly speaking, I think of writing DNA as purposefully converting other forms of information—such as pictures, movies or biological states—into sequences that can be stored and read out later. Many of these new writing technologies are driven by gene-editing systems derived from clustered regularly interspaced short palindromic repeats (CRISPR). With rationally engineered CRISPR systems, scientists can write DNA sequences.

DOUBLE-HELIX structure of DNA makes for an ideal storage medium. But it is not yet able to replace traditional hard drives.

GETTY IMAGES

Several of the most recent advances exploit the way CRISPR systems naturally evolved to defend bacteria against viral attacks. More specifically, viruses attack bacteria by binding onto the bacterial surface, then inserting their viral DNA or RNA. To "remember" the virus for future attacks, bacteria evolved CRISPR systems that identify viral DNA or RNA and then insert small snippets of the DNA into their own genome. In other words, the bacteria are "writing," or "recording," a history of the viruses that have attacked them to defend themselves.

By exploiting this mechanism, Seth Shipman, working in the lab of Harvard geneticist George Church and now at the University of California, San Francisco, used CRISPR to record images of a human hand directly into the genome of *Escherichia coli*. To accomplish this task, Shipman and his colleagues first expressed two proteins: Cas1 and Cas2. Together these proteins can acquire DNA nucleotides and insert them into the genome. The researchers then "fed" *E. coli* DNA sequences that encoded for pixels that—when sequenced together—created the image of a hand. Doing so required the scientists to assign different aspects of information to DNA. For example, in one case, A, C, G and T each stood for a different pixel color, whereas an associated DNA bar code sequence encoded the spatial position of the pixel within the entire image.

By sequencing the DNA from the *E. coli,* the authors then recapitulated the original image with more than 90 percent accuracy. Next, they repeated the experiment but with an important twist: they added the DNA at different times and included a method to analyze the position of the recorded DNA sequences, relative to one another. By measuring whether the sequences were added into the *E. coli* genome earlier or later, they were able to create a series of images, thereby encoding a movie. The researchers re-

corded a GIF from a part of the first motion picture, which was created by Eadweard Muybridge in 1878 and depicted a galloping horse. In a 2017 paper, they showed that they had reconstituted Muybridge's famous movie by sequencing the bacterial genome.

Even more recently, scientists in the lab of Randall Platt at the Swiss Federal Institute of Technology Zurich (ETH Zurich) made a critical discovery that takes these approaches even further by targeting mRNA, which is a key molecular cousin of DNA. Instead of recording images encoded by unnatural DNA sequences, they used a CRISPR system from a different bacterial species to generate so-called living records of natural mRNA gene expression in bacteria. The combination of all the different mRNAs in a cell dictates which proteins are made and therefore all cellular function.

To record mRNA produced by a cell at different time points, scientists at Platt's lab first screened CRISPR-Cas proteins derived from many different bacterial strains. This process allowed them to identify proteins capable of converting natural mRNA into DNA and encoding it into the genome. They found that Cas1 and Cas2 proteins from the bacterium *Fusicatenibacter saccharivorans* were capable of doing so. Through a series of elegant studies using specialized viruses, the team demonstrated in 2018 that the cells accurately recorded whether they had been previously exposed to oxidative stress, acidic conditions or even an herbicide.

These results were extremely exciting because they demonstrated that the genes naturally expressed by a cell at a given time could be recorded into the genome for later analysis. As Platt's lab continues to improve this technology, it is increasingly feasible that cellular recording could become commonplace. This development would enable scientists to track how a cell has become cancerous, responds to infection over time and even ages.

THE UBIQUITY OF DNA STORAGE

AS DNA IS USED to generate, track and store information in an increasing number of fields, the most obvious question is whether DNA will eventually compete with conventional electronic storage devices to maintain all the digital data humans generate. Currently the answer is no—hard drives and flash memory devices are far better at keeping information than even the most advanced DNA systems.

But like all technologies, conventional electronic devices have limitations. They take up physical space and require specific environmental conditions; even the most durable ones are unlikely to survive more than a few decades. Given these issues, it may soon become hard to maintain all the data we are generating today.

DNA, by comparison, could almost certainly last tens of thousands of years if kept in cool, dry conditions. It is already routinely stored at −20 or even −80 degrees Celsius in labs that require very cold conditions and can also be stored in the kind of extreme heat that typical electronics cannot withstand. In 2015 Robert Grass and Wendelin Stark, both at ETH Zurich, showed that DNA stored in silica could withstand 70 degree C temperatures for a week without introducing any errors. And although hard drives can fit as much as one terabit per square inch, recent estimations suggest that all the information generated in the entire world could theoretically be held in less than a kilogram of DNA.

There are still significant technological advances that need to be overcome for DNA storage to become commonplace. The primary limitation is that storing information is not identical to extracting it. Getting data from a hard drive is nearly instantaneous; extracting them from DNA requires sequencing, which currently takes a few minutes to a day to complete. And despite huge leaps in DNA sequencers over the past few years, they remain large and expensive as compared with hard drives.

These barriers are not the only considerations we must tackle before DNA storage can reach its full potential. As a society, we need to acknowledge that the ubiquity of DNA sequencing will also mean that it will become even easier to track people while generating new vulnerabilities for data security. Examples of privacy concerns abound, both in the U.S. and globally.

DNA sequencing is already being used by police departments across the U.S. with little oversight. By asking people who are under arrest—even for minor crimes—for their DNA, the police are establishing large data banks of genetic information. Some have argued this is the 21st-century equivalent of old-fashioned fingerprinting, but there is a critical difference. Fingerprints identify a single individual; if one of your relatives provides his or her DNA, that person is releasing information that can identify you or anyone else in your family. In China, under the guise of a health program, officials have gathered genetic information from nearly 36 million people. This population includes many Uighurs—members of a Muslim ethnic group that experiences discrimination. It remains unclear how these data will be used by the government.

Currently these concerns around DNA storage involve a person's genetic code itself—the discussion has been around protecting identity. But in the future, if other categories of information such as health care data, legal contracts and individual digital histories were stored in DNA, this scenario would launch even more questions about the vulnerability of DNA storage in the realms of both physical security and cybersecurity. Because so much information can be held in such a tiny space, how will data be distributed to avoid too much concentration in a single place? And even if extraction can be streamlined, how will data be routinely accessed and returned without exposing them to malicious hacks or accidental loss?

When I consider all the hard work—both scientific and ethical—that needs to be accomplished, it can seem daunting. I like to think about the Wright brothers because I grew up in the same Ohio town they did. Their first flight lasted 12 seconds and 37 meters. Sixty-six years later, without the advantages of modern computing, humans landed on the moon. These feats make me optimistic that we can harness the natural power of DNA over the next few decades and, by actively acknowledging its capability to do harm, help to ensure it mostly does good. SA

MORE TO EXPLORE

Next-Generation Digital Information Storage in DNA. George M. Church et al. in *Science,* Vol. 337, page 1628; September 28, 2012.

High-Throughput In Vivo Screen of Functional mRNA Delivery Identifies Nanoparticles for Endothelial Cell Gene Editing. Cory D. Sago et al. in *Proceedings of the National Academy of Sciences USA,* Vol. 115, No. 42, pages E9944–E9952; October 16, 2018.

Transcriptional Recording by CRISPR Spacer Acquisition from RNA. Florian Schmidt et al. in *Nature,* Vol. 562, pages 380–385; October 18, 2018.

FROM OUR ARCHIVES

Tech Turns to Biology as Data Storage Needs Explode. Prachi Patel; ScientificAmerican.com, published online May 31, 2016.

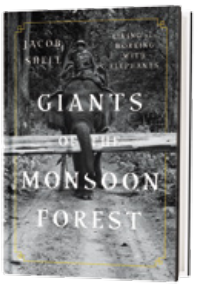
scientificamerican.com/magazine/sa

RECOMMENDED

By Andrea Gawrylewski

Giants of the Monsoon Forest: Living and Working with Elephants

by Jacob Shell. W. W. Norton, 2019 ($26.95)

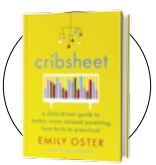


TRAINER works with a Sumatran elephant in Way Kambas National Park in Indonesia.

Asian elephants go where roads cannot. Their talent for navigating difficult terrain, coupled with their strength and smarts, has led humans to seek them out as cavalry and work animals for centuries. In rich detail, geographer Shell recounts this history and describes all the ways pachyderms collaborate with humans—for example, as draught animals for logging companies along the Indian-Burmese border and with Kachin Independence Army fighters, who run the world's only existing bureaucratically administered elephant-based transportation network. Shell meets Indian *mahouts*—or elephant keepers—and the animals themselves, which have unique personalities and striking intelligence. Ultimately Asian elephants' numbers are declining, primarily as a result of human activity—through either poaching or habitat destruction. Shell calls for a conservation strategy that involves the very people who engage with the creatures in the remote forests they call home. *—Jim Daley*

Cribsheet: A Data-Driven Guide to Better, More Relaxed Parenting, from Birth to Preschool

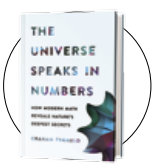
by Emily Oster. Penguin Press, 2019 ($28)



To swaddle or not to swaddle? Just one of the questions that comes up for parents of small children. Amid thousands of tomes, few offer such data-driven advice with so little agenda. Economist Oster evaluates the research on such hot-button issues as nursing, baby sleep and feeding to help parents make evidence-based decisions. For instance, breastfeeding is beneficial but perhaps less so than many claim; letting infants cry it out will not cause long-term damage; and there are good reasons to choose a nanny or day care, depending on your situation. Oster aims to "take some of the stress out of the early years by arming you with good information and a method for making the best decisions for your family." *—Clara Moskowitz*

The Universe Speaks in Numbers: How Modern Math Reveals Nature's Deepest Secrets

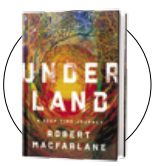
by Graham Farmelo. Basic Books, 2019 ($30)



Mathematics supplies invaluable clues to our understanding of the universe. Likewise, physics discoveries have often revealed new concepts in math. Yet not all physicists agree about how central math should be—some prefer the less abstract method of experiment and observation. Physicist Farmelo argues for placing math at the forefront, citing a legacy that goes back to Newton. For example, Einstein realized he needed to embrace advanced differential geometry to work on 4-D spacetime. And Emmy Noether discovered a connection that linked mathematical descriptions of nature and experimental results. Farmelo shows that theoretical physics and pure mathematics thrive best together. *—Sunya Bhutta*

Underland: A Deep Time Journey

by Robert Macfarlane. W. W. Norton, 2019 ($27.95)



Learning is often symbolized by light and height—a bulb switching on, a bird's-eye view or a flashlight carving away shadow. Writer Macfarlane takes the opposite tack, searching for answers in the deep and the dark. In this visceral, haunting travelogue through caves and catacombs and into glaciers and underground rivers across Europe and the Arctic, the author illustrates how humans have long relied on the underworld "to shelter what is precious, to yield what is valuable, and to dispose of what is harmful." From burial rituals and ghost cities to deep-sea oil rigs and tombs for nuclear waste, Macfarlane explores how societies have been molded by the subterranean landscapes on which they are built—and how humans are poised to stamp an unprecedented legacy deep into the earth's geologic memory. *—Frankie Schembri*

ULET IFANSASTI *Getty Images*

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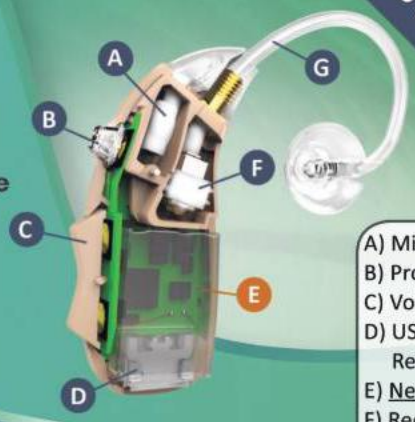

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Online Voting? Fuhgeddaboudit!

Tech experts can't guarantee it's safe

By Zeynep Tufekci

Online voting sounds like an idea we should be able to make work. After all, we do so much online already, and we routinely transmit sensitive data such as financial or medical records by encrypting them. Further, there are cryptographic methods, called end-to-end verifiability, that promise citizens that their votes are recorded as they intended; that each vote is tallied; and that the final tally is the sum of all the ballots. Plus the convenience of online voting may spur more participation in elections.

And where better to try online voting than in Switzerland, where people vote early and often? Although the Swiss have a traditional parliament, many consequential decisions are voted on directly by the people. Unsurprisingly, this results in lots of elections! In just 2018 the Swiss held 10 different referendums on a variety of topics. Voting that much makes the Swiss even more sensitive to electoral convenience than we are.

There is already limited online voting in some Swiss cantons, using two separate certified systems. The government says two thirds of those eligible have chosen this option, attesting to the demand. When the country decided recently to try to dramatically expand online voting, they proceeded methodically in true Swiss fashion. The first step was to hold a mock referendum and invite the world's "white hat" hackers—security researchers who expose vulnerabilities so that they can be fixed—to infiltrate the system, offering about $150,000 in rewards and bragging rights.

Zeynep Tufekci is an associate professor at the University of North Carolina School of Information and Library Science and a regular contributor to the *New York Times*. Her book, *Twitter and Tear Gas: The Power and Fragility of Networked Protest*, was published by Yale University Press in 2017.

The rewards were swiftly claimed. Three independent teams showed that hackers could alter vote results undetected—the worst-case scenario. The flaw pertains to the way that the system "shuffles" the encrypted votes to protect voter privacy before tallying. This is fixable. But even if it's fixed, how can voters be fully assured that they should trust the new system?

And therein lies the biggest flaw in all e-voting schemes: the ones that don't employ cryptography cannot provide the crucial guarantees of secret balloting and verification of tallies. And those that *do* use cryptographic schemes require that the voters trust the experts. Estonia, a country that has used online voting since 2005, is a case of the latter. A team of researchers at the University of Oxford that examined Estonia's system in 2016 praised many of its safety procedures but noted that because of the country's small size, officials also rely on building trust among people who run their elections through interpersonal relationships. Estonians seem to think that's good enough—but it's not an easy model to export.

Another thing that distinguishes Estonia is a mandatory digital ID system: every Estonian citizen is issued a card with cryptographic keys widely used for both public- and private-sector functions. While that solves one problem—how to identify voters and prevent double voting—it creates another: such systems can also function as a vast tracking and surveillance system that other countries may not be comfortable with.

Digital IDs can create a third problem: in 2017 a weakness was found in the hardware in Estonian cards, potentially allowing identity theft—the very thing the card is supposed to prevent. Officials quickly replaced the cards and upgraded their systems, but a real crisis was averted only because the flaw wasn't actually exploited. Next time, that might not be the case.

In the end, the biggest flaw in even the most secure online voting system is this: trusting the experts isn't supposed to be how voting works. It's true that voter fraud and errors can occur in a variety of systems, but electronic voting lowers the bar for both stealthiness and scale. Paper ballots can definitely be corrupted, but that requires organizing lots of people in a secret scheme that is hard to keep under wraps. And if fraud is suspected, you can just do a recount in the presence of eagle-eyed observers.

Trust in election results is the bedrock of any democratic government's legitimacy. Online voting systems cannot fully assure citizens that there are no trapdoors, backdoors, bad implementations or weaknesses. Instead of online voting, democracies should focus on making voting convenient through other measures: national holidays on election days, increasing the number of polling places, sufficient numbers of voting machines to decrease lines, transportation to the booth for people who need it, and more. Voting is too important for systems that rely on "trust the experts" schemes. SA

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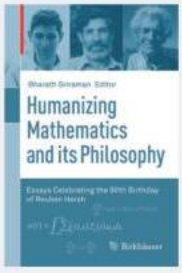
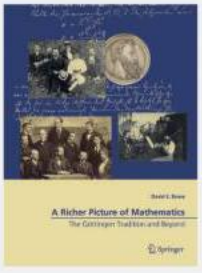
Illustration by Christina Chung

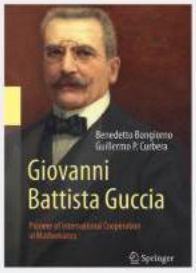
Mathematics Highlights from Springer



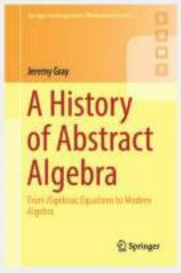
B. Sriraman
Humanizing Mathematics and its Philosophy
Essays Celebrating the 90th Birthday of Reuben Hersh
2017



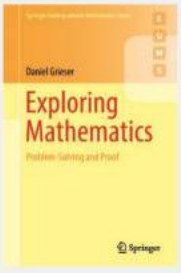
D. E. Rowe
A Richer Picture of Mathematics
The Göttingen Tradition and Beyond
2018



B. Bongiorno, G. P. Curbera
Giovanni Battista Guccia
Pioneer of International Cooperation in Mathematics
2018

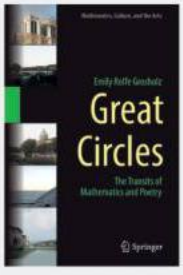


J. Gray
A History of Abstract Algebra
From Algebraic Equations to Modern Algebra
2018

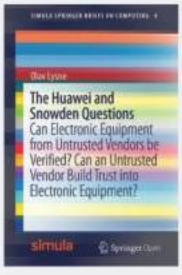


D. Grieser
Exploring Mathematics
Problem-Solving and Proof
2018

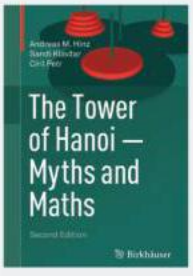
S. S. Cottrell
Do Colors Exist?
And Other Profound Physics Questions
2018



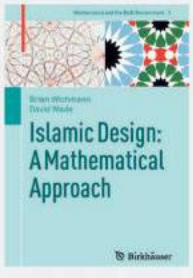
E. R. Grosholz
Great Circles
The Transits of Mathematics and Poetry
2018



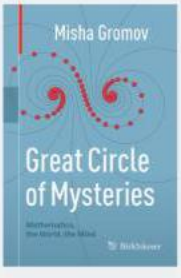
O. Lysne
The Huawei and Snowden Questions
Can Electronic Equipment from Untrusted Vendors be Verified? Can an Untrusted Vendor Build Trust into Electronic Equipment?
2018



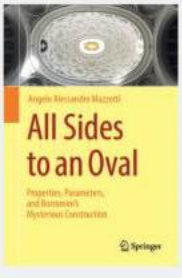
A. M. Hinz, S. Klavžar, C. Petr
The Tower of Hanoi – Myths and Maths
2nd ed. 2018



B. Wichmann, D. Wade
Islamic Design: A Mathematical Approach
2017



M. Gromov
Great Circle of Mysteries
Mathematics, the World, the Mind
2018



W. P. Ziemer
All Sides to an Oval
Properties, Parameters, and Borromini's Mysterious Construction
2017

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.

Calculust

A new book that can make you love calculus

By Steve Mirsky

The great Greek scientist, engineer and mathematician Archimedes left us two quotes that ring through the centuries. His study of levers is said to have led him to remark, "Give me a place to stand, and I will move the world." And the famous *Eureka!* ("I have found it!") came from his discovery, allegedly while taking a bath, that the volume of an irregularly shaped object could be determined by submerging it and measuring how much water it displaced. Sadly, there's no evidence that he ever uttered the mash-up "Give me a place to stand, and I will take a shower." Which seems like an Archimedes screwup.

Archimedes gets lionized (but Androcles is not mentioned) in the new book *Infinite Powers: How Calculus Reveals the Secrets of the Universe,* by Cornell University professor of applied mathematics Steven Strogatz. For anyone who vowed that their calculus textbook would be the last thing they'd ever read on the subject, reconsider: "I've written *Infinite Powers* in an attempt to make the greatest ideas and stories of calculus accessible to everyone," Strogatz notes in the introduction. Then, throughout the book, he gently explains the basics—and gives a historical context that makes for a fascinating read even if you skip the math parts completely. Like you may have done with your textbook.

The history includes the fact that the word "calculus" comes from the Latin root *calx,* meaning a "small stone." "A reminder of a time long ago," Strogatz writes, "when people used pebbles for counting and thus for calculations.... Doctors use the same word for gallstones, kidney stones, and bladder stones." In my younger days, I studied derivatives and integrals, but I don't recall learning until I read *Infinite Powers* that both of the two 17th-century geniuses usually credited with the invention of calculus, Isaac Newton and Gottfried Wilhelm Leibniz, "in a cruel irony ... died in excruciating pain while suffering from calculi—a bladder stone for Newton, a kidney stone for Leibniz." At least it was just hyperbole if you ever complained in school that calculus was killing you.

Calculus deals with a lot of curves, and Strogatz thinks of the development of calculus as curvy. No question, Newton and Leibniz gave the field a tremendous acceleration. But the stuff before them was not protocalculus, as it's often portrayed: "To me," he writes, "it's been calculus all along, ever since Archimedes harnessed infinity."

So how did old Archie yoke that enormous ox without getting gored? He, and his followers after him, used what Strogatz calls the infinity principle: "To shed light on any continuous shape, object, motion, process, or phenomenon—no matter how wild and complicated it may appear—reimagine it as an infinite series of simpler parts, analyze those, and then add the results back together to make sense of the original whole."

For Archimedes, employing the principle meant determining a circle's circumference (its diameter multiplied by pi) by thinking of it as an infinite number of infinitely short straight lines. Start with just six lines, and you get a value for pi of 3. Get to a mere 96 lines, and you know that pi is between $3 + {}^{10}/_{71}$ and $3 + {}^{10}/_{70}$. Not bad for a back-of-the-parchment appraisal.

What evolved over the millennia became the math that gave us modernity. "Without calculus, we wouldn't have cell phones, computers, or microwave ovens," Strogatz writes. "We wouldn't have radio. Or television. Or ultrasound for expectant mothers, or GPS for lost travelers. We wouldn't have split the atom, unraveled the human genome, or put astronauts on the moon."

And thanks to calculus, you can use your microwave oven, a flat plate and some grated cheese to get a shockingly good estimate of the speed of light. That recipe is in chapter 10, "Making Waves." And after doing the experiment, you can eat the cheese. Which is a good source of calcium, another word that comes from *calx.* Also tracing its origin to *calx* is caulk, a handy substance to keep around should you make any world-shaking discoveries in the bathtub. SA

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Illustration by Matt Collins

50, 100 & 150 YEARS AGO

INNOVATION AND DISCOVERY AS CHRONICLED IN *SCIENTIFIC AMERICAN*

Compiled by Daniel C. Schlenoff

JUNE

1969 Heart-Healthy Water

"Several studies in the past decade have suggested that the death rate from coronary disease is inversely correlated with the hardness of the local water supply: the harder the water, the lower the coronary rate. A study recently published in *The New England Journal of Medicine* reports evidence that the excess coronary deaths in soft-water areas are almost entirely sudden deaths outside the hospital. Researchers at the University of Toronto School of Hygiene reviewed the death certificates of 55,000 people who died in the province of Ontario in 1967 and classified the deceased individuals according to the hardness of their local water supply."

The reason for the link is still under debate; latest theories suggest more magnesium and calcium are beneficial.

Rubella Vaccine

"Vaccines that have produced immunity against rubella ('German measles') in more than 95 percent of the test subjects who have received them will probably be licensed in the U.S. within a matter of weeks. Widespread immunization with these vaccines could prevent another wave of infection, anticipated for the early 1970s, like the one that swept across the U.S. in 1964, causing at least 8,000 fetal deaths and afflicting 15,000 to 20,000 infants with deafness, heart disease, cataracts, glaucoma, psychomotor retardation and blood disorders."

1919 Transatlantic Flight at Last!

"Search through the history of all the arts and sciences, and you will find none that has furnished so much of the sensational and the heroic as the latest of them all: the art of flying—that amazing child of the Twentieth Century. A land bird, scorning its native element, had swept across the Atlantic from Newfoundland to the Irish Coast in one wild flight of sixteen hours and a half. The Vickers-Vimy bomber, which carried Captain Alcock on his amazing dash, was built to bomb Berlin. The landing was made within a few miles of the place selected by Navigator Brown. So these gallant lads, who had lunched in America, had their breakfast, next day, in Europe."

Glacial Progress

"Another of the leading scientific societies of Great Britain, the Geological Society, has decided to admit women as fellows. This step has been considered by the society on three previous occasions, with negative results."

1969

1919

1869

1869 Circular Cycling

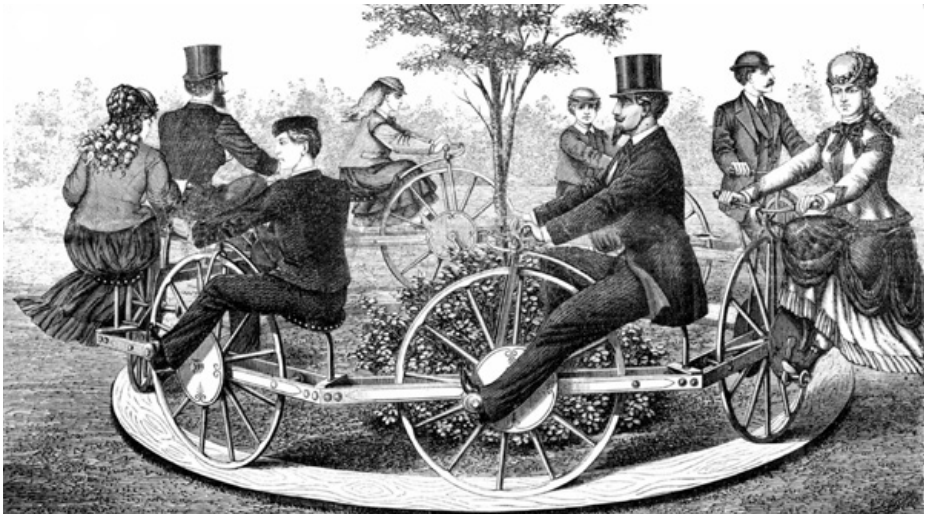
"A velocipede adapted to the use of all, old or young, large or small of either sex, skilled or unskilled, in which the pleasure of the exercise is enhanced by association, is shown in our engraving. The action and details of this invention are well delineated by our artist. This machine is designed for use in private and public pleasure grounds, or to be let by the hour at large fairs. It does one's heart good, says our enthusiastic informant, to hear children fairly shriek with glee as the maximum speed is attained."

Magnetic Storm

"On the evening of the 15th of April a magnetic storm of unusual force prevailed over the entire northern section of the country, which so seriously affected the operation of the wires that, on some circuits, they could only be worked by taking off the batteries and employing the auroral current instead. The effect of this great disturbance of the earth's magnetism was manifested with particular power upon the wires between New York and Boston, and for several hours the lines upon this route depended entirely upon this abnormal power for their working current."

Paper for the Nose

"The Japanese dignitaries, says the *Boston Journal of Chemistry,* who recently visited this country under the direction of Mr. Burlingame, were observed to use pocket paper instead of pocket handkerchiefs, whenever they had occasion to remove perspiration from the forehead, or 'blow the nose.' The same piece is never used twice, but is thrown away after it is first taken in hand. We should suppose in time of general catarrh, the whole empire of Japan would be covered with bits of paper blowing about. The paper is quite peculiar, being soft, thin, and very tough."



1869: Forerunner of the spin class (sidesaddle for the ladies).

SCIENTIFIC AMERICAN, VOL. XX, NO. 23, JUNE 12, 1869

Text by Mark Fischetti | Graphic by Lisa Mahapatra

Follow the Water

Solving global water issues will greatly benefit food and energy, too

The United Nations Sustainable Development Goals are intended to create a world that is socially, economically and environmentally fair and resilient. But there are 17 goals and 169 actions ("targets") within them. Where should a country begin, especially if it has limited resources? Sustainability experts say that the goals of water, food and energy are crucial to the wider set and that they are tightly intertwined. A new analysis by four international researchers indicates water solutions provide the greatest synergistic advantages for all three (*large graphic*) and have only a few minor problematic trade-offs (*small graphic*). "We want policy makers to see that these goals have to be achieved together," says Marianela Fader, deputy director of the International Center for Water Resources and Global Change in Germany. "And that water pays off best."

Positive Synergies

Pursuing certain targets within the U.N. Sustainable Development Goals for water, food and energy (*numbered with their official designations*) reinforces progress in others. Overall, water targets have the greatest benefits.

Synergy with Other Targets

+3 (strong)
+2
+1 (mild)

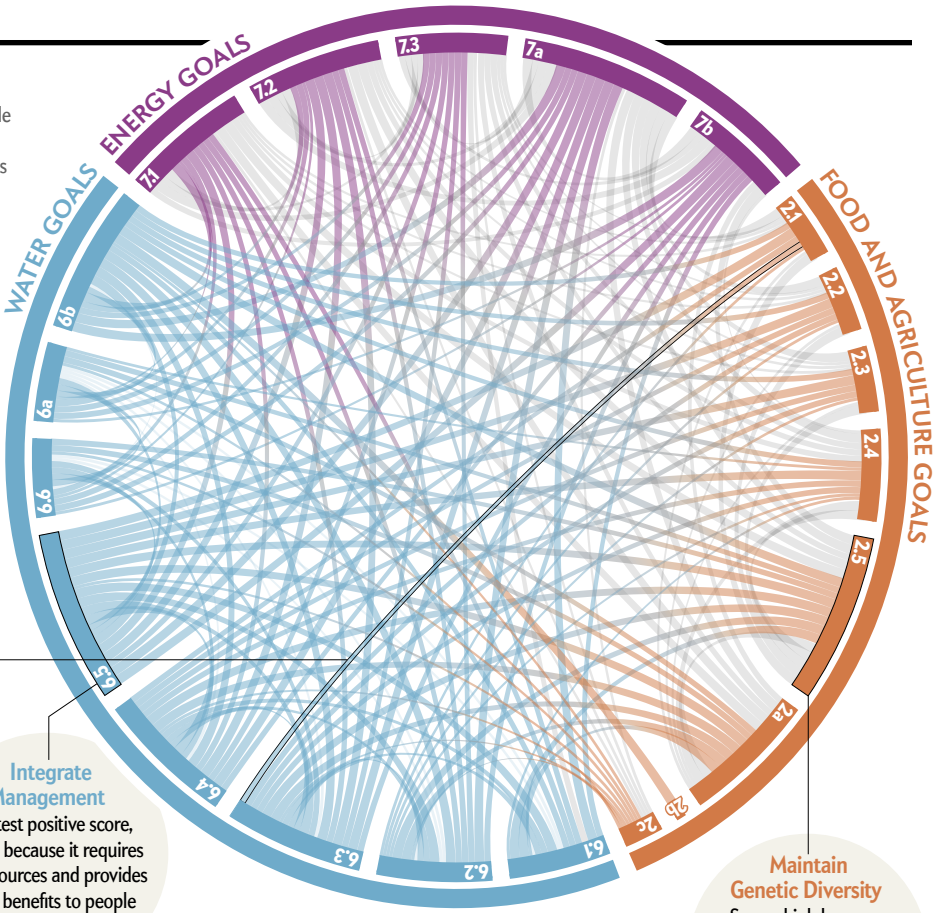
Water–Water
Water–Energy
Water–Food
Synergy does not involve water

Synergy Strength Calculated

Pairs of targets were evaluated against eight criteria. For each criterion, a mutual benefit between the pair scored +1, and a negative trade-off scored –1. The sum of the eight scores gave a total, shown in the circles as the width of the line connecting the pair. For example, targets 2.1 and 6.3 had three synergies (+3), one trade-off (–1) and four neutral interactions (0), totaling +2.

Criteria Assessed

The eight criteria were: water needs; land and soil needs; electricity and fuel needs; need for roads, pipes and other gray infrastructure; need for education and technology infrastructure; need for health care; and benefits and risks for ecosystem services to people and to the planet.



Integrate Management
Greatest positive score, largely because it requires few resources and provides many benefits to people and ecosystems.

Maintain Genetic Diversity
Scores high because it is crucial to numerous food and water targets and presents no complication for any other target.

ENERGY GOALS
- 7.1 Make access affordable
- 7.2 Expand renewable sources
- 7.3 Improve efficiency
- 7a Transfer technology
- 7b Modernize infrastructure

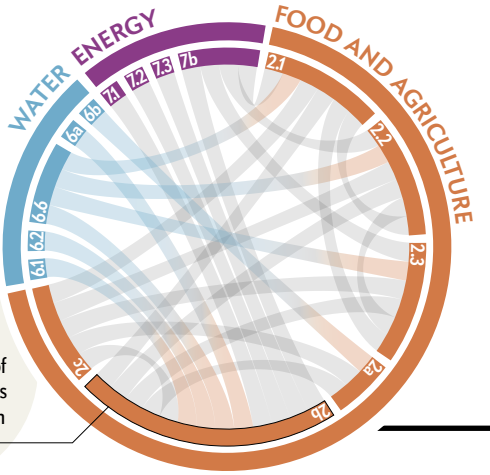
FOOD AND AGRICULTURE GOALS
- 2.1 End hunger
- 2.2 End malnutrition
- 2.3 Double productivity
- 2.4 Produce sustainably
- 2.5 Maintain genetic diversity
- 2a Invest in rural agriculture
- 2b End market interference
- 2c Improve commodity markets

WATER GOALS
- 6.1 Make drinking water safe
- 6.2 Provide adequate sanitation
- 6.3 Improve quality
- 6.4 Increase efficiency
- 6.5 Integrate management
- 6.6 Restore ecosystem
- 6a Cooperate internationally
- 6b Involve local communities

Negative Trade-offs

Pursuing one target can undermine another. Several water, food and energy targets had one counterproductive trade-off. Yet most of them had more than one positive synergy (*larger graphic*), offsetting the complication. (*Circle enlarged for legibility.*)

Negative Relationship with Other Targets: –1 (mild)



End Market Interference
Greatest negative score, largely because of environmental problems such as soil degradation and deforestation.

SOURCE: "TOWARD AN UNDERSTANDING OF SYNERGIES AND TRADE-OFFS BETWEEN WATER, ENERGY, AND FOOD SDG TARGETS," BY MARIANELA FADER ET AL., IN *FRONTIERS IN ENVIRONMENTAL SCIENCE*, VOL. 6, ARTICLE 112; NOVEMBER 18, 2018

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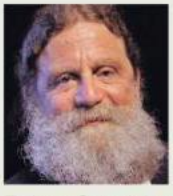

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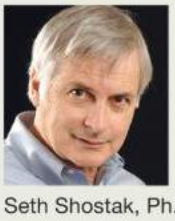

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