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Giant stars explode in a myriad of ways, recent discoveries show. Astrophysicist Anna Y. Q. Ho surveys several unusual supernovae sighted recently and explores what they can teach us about how stars live and die. **Illustration by Kenn Brown.**

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FROM THE EDITOR

The Human Side of Science

One of the joys of being a science journalist is that it's your job to talk with people who are doing mind-bending and world-changing research and to ask them goofy questions. We ask them serious questions, too, of course, but we also encourage scientists to share the funny, tense, disappointing, surprising, human sides of their work. The goal is not to make an expert seem ridiculous but to demonstrate that we're all just people trying to figure out how to make sense of the world.

This month's cover story on new discoveries about how stars explode and die is an exciting look at a rapidly growing field that is studying phenomena at awesome time and size scales. But it's also a human drama about how Anna Y. Q. Ho had to sleep in a sleeping bag in a remote observing lab, wake up at 4 A.M. and race the dawn to get a reading on an exploding star 21 billion light-years away. See page 26 for more about her pursuit of strange star endings.

One reason we urge scientists to show us the personal side of research is that we hope it demystifies what they do. Increasingly, we're seeing the danger of people rejecting scientific findings and claiming that certain fields are all a hoax or a conspiracy. It's distressing but mostly harmless when people fall for fake documentaries claiming the earth is flat. It's life-threatening when they fall for misinformation about the COVID-19 pandemic. Starting on page 54, Filippo Menczer and Thomas Hills detail the ways conspiracy theories spread—including a



Laura Helmuth is editor in chief of *Scientific American*. Follow her on Twitter @laurahelmuth

disinformation campaign targeted at their own research group.

The delicate surgery required to transplant a hand is just the start of the process; the recipient must then relearn how to use it. The brain reroutes neural signals in many different areas, showing how nimble and adaptable it can be. Scott H. Frey describes how his early interest in neuroscience was inspired by his mother's multiple sclerosis and her loss of motor control. He shares this research starting on page 62.

The human body is actually a superorganism teeming with bacteria, fungi and hundreds of trillions of viruses. The study of the human virome is only about a decade old, and the research is accelerating as scientists respond to SARS-CoV-2, the virus that causes COVID. These viruses aren't all bad. Some are harmless, and some might help treat diseases or fight antibiotic resistance. Turn to page 46 for David Pride's fascinating discoveries about the viruses that live in and among us.

The idea of an international collaboration to build a fusion reactor that could produce clean energy came out of a Superpower Summit in Geneva in 1985 featuring Ronald Reagan and Mikhail Gorbachev. Now the International Thermonuclear Experimental Reactor is being built. The project feels like a series of marathons, the ITER director tells senior editor Clara Moskowitz. Parts have been made all over the world, and beginning on page 70, you can see the stunning facility coming together.

We're delighted to have editor in chief emerita Mariette DiChristina back in our pages this issue. Once again, she and the World Economic Forum teamed up with a steering committee of experts in a wide range of fields to highlight 10 emerging technologies (*page 34*). It's an inspiring package and a reminder that research and innovation have the potential to save and improve our lives.

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August 2020

BIOMASS APPEAL

In "The Biomass Bottleneck," Eric Toensmeier and Dennis Garrity address the strategy of drawing down billions of tons of carbon dioxide by using biomass for energy and carbon capture. Their analysis concludes that the amount of biomass required would leave the world with inadequate arable land to grow food. And they indicate that available biomass waste that currently has no other use is not available in sufficient quantity to make a significant dent in the climate change crisis.

I wish to call attention to a recent analysis by a consortium of scientists collaborating with Lawrence Livermore National Laboratory entitled Getting to Neutral: Options for Negative Carbon Emissions in California. The goal of this work was to create a cost-effective plan to bring California to carbon neutrality by 2045. In the report, the biggest contributor to attaining this goal is the conversion of waste biomass to fuels. The CO₂ generated in producing such fuels can then be sequestered underground, leading to a net removal of CO2 from the atmosphere without impacting food production. I also wish to make the general point that some fraction of the biomass that is currently used for certain applications, such as animal feed, might need to be directed to clean energy generation and carbon capture in a carbon-constrained future.

I wholeheartedly agree with the authors that improvement in agricultural

"Solving the climate crisis will require many different activities, whose nature can vary with geographical location."

JOFFRE BAKER MONTARA, CALIF.

practices is profoundly important. Solving the climate crisis will require many different activities, whose nature can vary with geographical location. Utilizing waste biomass can play a significant role in allowing California to achieve its goal of carbon neutrality.

JOFFRE BAKER Montara, Calif.

Toensmeier and Garrity omit an important variable in their discussion of the potential for biomass energy. If people were to adopt a plant-based diet, the amount of agricultural land needed for food production would be greatly reduced. When crops are fed to animals, the loss of efficiency is staggering. And cattle are a major source of methane emissions. If people ate less meat, much existing cropland could be used for biomass energy with no harm to human welfare.

> M. BARTON LAWS Brown University School of Public Health

LAST HUMAN STANDING

In "Survival of the Friendliest," Brian Hare and Vanessa Woods imply that a lack of friendliness led to the extinctions of at least four other known human species that were mutually extant with our own. But there are anthropologists who attribute our singular success to pursuing the genocidal destruction of all the other competing species. Similarly, many present-day religions claim superiority over all other competing religions, often seeking to eliminate the competition. Is there a genetic linkage between species domination and religious domination?

Roy Bruno Redmond, Wash.

The authors refer to our species succeeding, but they never directly define what human success is, unless it is some crude Darwinian measure of reproduction and the displacement of other species. We can look around and see the impact of the "success" of eight billion people: We have the capacity for culture and can cooperate. Yet our cooperation has been used to wage war and commit genocide (even slaughtering people halfway across the globe); to cause extinctions and greatly diminish the numbers of other species; to turn complex ecosystems into monocultures; and to wreck a planet's climate. We have lost the ability to control the narcissists we produce. If this is cultural prowess and success, let's say that the story is not over yet. And it does not seem particularly friendly. There is good evidence we have become less emotionally mature as a species.

DAVID JOHNS McMinnville, Ore.

RACE AND COVID-19

Thank you for "Black Health Matters," by the Editors [Science Agenda], as well as the powerful imagery used to visually highlight the discrepancy in health care as it pertains to race. The illustration should be hung in research institutions and policy-making rooms around the country.

I agree that many of the health care disparities stem from systemic racism and policies, such as those that prevented Black people, in particular, from purchasing Federal Housing Administration-insured mortgages in our country until 1968-forcing many to live in segregated and overcrowded communities that have now become a breeding ground for pandemic-related illness. As a result of these policies, neighborhood schools became rife with underfunded, poor-quality education. That problem, in turn, led to the inability of many of those neighborhoods' residents to access higher education or jobs with decent wages, and they had far fewer opportunities to receive adequate health insurance and health care. The result was a reduced ability to learn about such health impacts as vitamin D deficiency, high blood pressure, and so on. Additionally, previously redlined neighborhoods have been surrounded by food deserts-with stores providing minimal access to fresh fruits and vegetables and rampant with an overabundance of processed and

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sugar-laden foods and drinks—which has led to disproportionate rates of type 2 diabetes. All these factors affect how Black and brown people are impacted by SARS-CoV-2, the virus that causes COVID-19.

I would love to see a recurring section of *Scientific American* that would analyze what information is available to doctors and scientists around the world pertaining to health consequences for Black and brown people. For example, you could examine the role that thrombosis plays in COVID-19 in this population and explain why, for many Black and brown individuals, the disease is vascular in nature rather than respiratory.

I concur that there will be another pandemic. And if all lives truly matter, addressing the science behind why COVID-19 is disproportionately affecting those of us in Black and brown communities will be one of the first steps in finding how to fix it and other ailments through the art of science. Imagine the impact an ongoing publication highlighting concurrent sociological and biological research on this population would have 20 years from now. And for those who don't care about the actual people being affected and whose primary concern is the impact on the economy, such information would inform how to keep businesses open and staffed with healthy employees because the frontline workers come predominantly from these communities.

Kelly Ector via e-mail

THE WAY I WALK

"Step Spy," by Sophie Bushwick [Advances; July 2020], reports on sensors that identify people by their walking gait, which is unique for each person. I had to laugh when I read the article! I am now 77 years old. When I was seven, my mother went out one day to visit a neighbor in our building. She told me not to answer the door to anyone but her. I was to make absolutely sure it was her before I answered the door. An hour later I heard her come down the stairs and approach the door, so I opened it. Of course, I was punished despite insisting that I *did* know it was her because I recognized her gait.

I can't undo the spanking I got, but after 70 years it feels good to be vindicated at last.

JUDY ANDERSON via e-mail

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Racism in Medical Tests

Many diagnostic assessments are inherently biased against people of color

By the Editors

COVID-19 has wreaked <u>havoc</u> on Black and Indigenous communities and other people of color, and U.S. medical institutions should be doing everything they can to root out and eliminate entrenched racial inequities. Yet many of the screening assessments used in health care are exacerbating racism in medicine, automatically and erroneously changing the scores given to people of color in ways that can deny them needed treatment.

These race-based scoring adjustments to evaluations are all too common in modern medicine, particularly in the U.S. To determine the chances of death for a patient with heart failure, for example, a physician following the American Heart Association's guidelines would use factors such as age, heart rate and systolic blood pressure to calculate a risk score, which helps to determine treatment. But for reasons the AHA does not explain, the algorithm automatically adds three points to non-Black patients' scores, making it seem as if Black people are at lower risk of dying from heart problems simply by virtue of their race. This is not true.

A recent paper in the New England Journal of Medicine presented 13 examples of such algorithms that use race as a factor. In every case, the race adjustment results in potential harm to patients who identify as nonwhite, with Black, Latinx, Asian and Native American people affected to various degrees by different calculations. These "corrections" are presumably based on the long-debunked premise that there are innate biological differences among races. This idea persists despite ample evidence that race-a social construct-is not a reliable proxy for genetics: Every racial group contains a lot of diversity in its genes. It is true that some populations are genetically predisposed to certain medical conditions-the BRCA mutations associated with breast cancer, for instance, occur more frequently among people of Ashkenazi Jewish heritage. But such examples are rare and do not apply to broad racial categories such as "Black" or "white."

The mistaken conflation of race and genetics is often compounded by outdated ideas that medical authorities (mostly white) have perpetuated about people of color. For example, one kidney test includes an adjustment for Black patients that can hinder accurate diagnosis. It gauges the estimated glomerular filtration rate (eGFR), which is calculated by measuring creatinine, a protein associated with muscle breakdown that is normally cleared by the kidneys. Black patients' scores are automatically adjusted because of a now discredited theory that greater mus-



cle mass "inherent" to Black people produces higher levels of the protein. This inflates the overall eGFR value, potentially disguising real kidney problems. The results can keep them from getting essential treatment, including transplants. Citing these issues earlier this year, medical student Naomi Nkinsi <u>successfully pushed</u> the University of Washington School of Medicine to abandon the eGFR race adjustment. But it remains widely used elsewhere.

A recent study in *Science* examined an algorithm used throughout the U.S. health system to predict broad-based health risks. The researchers looked at one large hospital that used this algorithm and found that, based on individual medical records, white patients were actually healthier than Black patients with the same risk score. This is because the algorithm used health *costs* as a proxy for health *needs*—but systemic racial inequality means that health care expenditures are higher for white people overall, so the needs of Black people were underestimated. In an <u>analysis of these findings</u>, sociologist Ruha Benjamin, who studies race, technology and medicine, observes that "today coded inequity is perpetuated precisely because those who design and adopt such tools are not thinking carefully about systemic racism."

The algorithms that are harming people of color could easily be made more equitable, either by correcting the racially biased assumptions that inform them or by removing race as a factor altogether, when it does not help with diagnosis or care. The same is true for devices such as the pulse oximeter, which is calibrated to white skin—a particularly dangerous situation in the COVID pandemic, where nonwhite patients are at higher risk of dangerous lung infections. Leaders in medicine must prioritize these issues now, to give fair and often lifesaving care to people left most vulnerable by an inherently racist system.

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David Shiffman is a marine conservation biologist, scientific consultant and science writer based in Washington, D.C.

How to Do Conservation the Right Way

The so-called 30 by 30 plan could make a huge difference—if enacted

By David Shiffman

No matter which party wins a presidential election, it's a good bet that its formal platform won't be fully enacted. Platforms are at least partly aspirational; they include proposals that are too radical, even in the eyes of some party members, to be enacted into policy or law any time soon. That could certainly be seen as the case with a plan called "<u>30 by 30</u>," which the Democrats put on their <u>official wish list</u> back in August: it calls for protecting 30 percent of U.S. lands and waters from development by the year 2030. It would, if implemented, represent the largest shift in biodiversity conservation policy since the Endangered Species Act was passed in 1973.

But the 30 by 30 idea isn't new, and it isn't radical eco-extremism run amok. It has been discussed for years by the sciencebased conservation community and has been vetted in peerreviewed journals, including *Science Advances*, and detailed reports from well-respected nonprofits such as Defenders of Wildlife and the Center for American Progress. A resolution in support of this goal has been introduced in Congress and in several state legislatures, including that of South Carolina—hardly a hotbed of far-left activism.

The 30 by 30 plan is based on a huge and growing body of scientific evidence that says that the world's wildlife and wild places <u>face existential threats</u>—and that a commitment to help save these places is good not only for the abstract goal of "protecting the environment" but also because it matters for people, too. According to Lindsay Rosa, a senior conservation scientist at Defenders of Wildlife's Center for Conservation Innovation, the most commonly cited figures suggest that about 12 percent of U.S. land and 26 percent of U.S. waters are currently protected but there is a lot of land that is important for biodiversity conservation that is not yet protected but could be.

Experts also emphasized that it matters *which* 30 percent we protect. Conserving a giant, undeveloped stretch of land where little lives and that no one wanted to develop anyway is not especially helpful to biodiversity conservation or climate resilience. We need to protect at least some of every major ecosystem, an ecological concept called representativity, as well as habitats where species of concern actually live.

When we are dealing with migratory species, for example, corridor conservation is critical to safeguard <u>their migratory routes</u> and not just their destination. Not all habitats are equally helpful



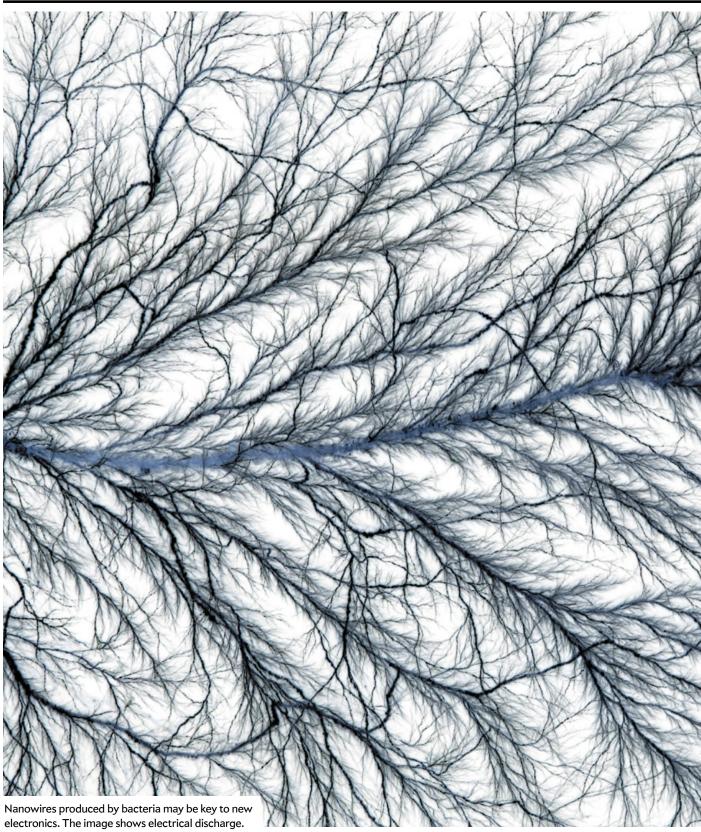
in terms of climate resilience. Moreover, human needs are vital when determining which habitats should be off-limits to largescale resource extraction and development. So whereas some topdown coordination is necessary, local voices would have to have a say, especially on lands inhabited by Indigenous people. And because unequal access to wild spaces and the mental and physical health benefits they provide is a <u>major environmental justice</u> issue, says Kate Kelly, public lands director at the Center for American Progress, 30 by 30 "is an opportunity to hit the reset button on who conservation is for and who nature can benefit."

Does such a bold plan have a chance of happening in our hyperpolarized government? It really might because conserving wildlife and wild places often has tremendous bipartisan support; in fact, 86 percent of voters somewhat or strongly support the specific goal of 30 by 30, including 76 percent of Republican voters, according to a poll conducted by the Center for American <u>Progress</u>. And, points out Justin Kenney, director of the 30x30 Ocean Alliance, President George W. Bush created what was at the time the largest marine protected area in the world.

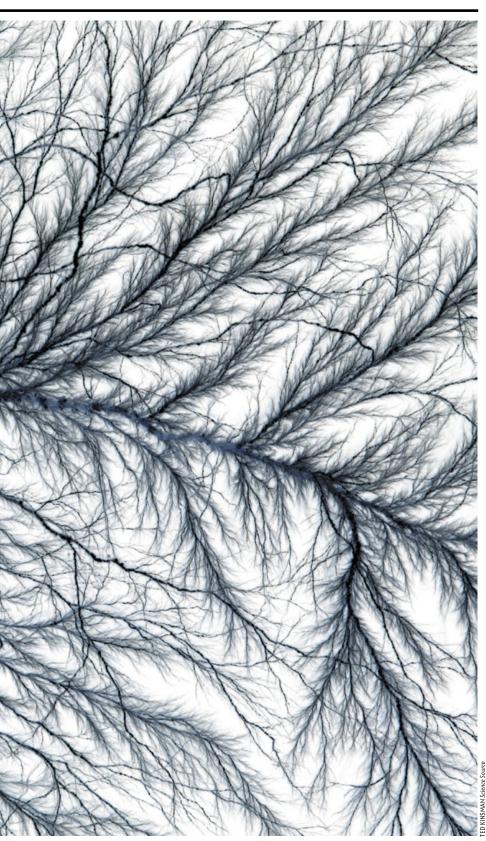
30 by 30 represents the last best hope for saving many of the U.S.'s iconic species and wild places and is a key step in fighting climate change and restoring ecological justice. But although such a plan is important, there is obviously no guarantee that it will happen. "We need continued U.S. leadership to reach the goal of 30 by 30," Kenney says, which isn't necessarily wise to count on. Still, he believes "it's gaining more and more momentum each day."

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DISPATCHES FROM THE FRONTIERS OF SCIENCE, TECHNOLOGY AND MEDICINE

INSIDE

- Ultracold molecules' behavior revealed
- Woodpecker spectators congregate to watch dramatic territory fights
- Sounds from underwater earthquakes help to measure ocean temperatures
- A 1920s sailing invention makes an energy-saving comeback

Live Wires

Scientists are decoding the mysteries behind microbes' electron-wicking nanowires

Bacteria in the genus *Geobacter* look like miniature kidney beans sprouting long, wirelike tails—and it turns out these "nanowires" really do <u>conduct electricity</u>. Scientists have been studying such conductive bacteria for decades, hoping to develop living technology that can work safely inside the human body, resist corrosion or even literally pull electricity out of thin air. But to make this practical, they first must unlock the mystery of how these minuscule fibers actually work—and a vigorous debate is shaping up.

Geobacter's conductive abilities were discovered by Derek Lovley, a microbiologist at the University of Massachusetts Amherst, who wanted to know how these bacteria rid themselves of the electrons produced during their energy-generation process. Most microbes need to pass electrons to adjacent oxygen molecules to "breathe"-but Geobacter thrives in oxygenfree environments. Lovley eventually realized that these one-celled organisms produce long chains of proteins that carry the electrons to nearby rust molecules, which use the charged particles to transform into magnetite. Other protein nanowires have been discovered since, but Lovley thinks one kind, called pili, plays a primary role. The proteins that make up pili-called pilins-are too small to investigate with traditional imaging technology, so Lovley demonstrated their importance by removing the gene for making pili. Without it, Geobacter could no longer change rust into

ADVANCES

magnetite. Furthermore, he found that pili he gathered from the cells could indeed conduct electricity.

Researchers have already developed applications that use living conductive microbes, but Lovley wants to harvest the nanowires themselves to build environmentally friendly electronics. He recently co-authored two papers on sensors made from Geobacter nanowires: One, described in Nano Research, detects ammonia; the other, detailed in Advanced Electronic Materials. picks up changes in humidity. Another device, which his group described in Nature, uses nanowires to pull electrons from water molecules in the air-thus producing electricity from humidity. "It has some advantages over the other sustainable forms of electricity production, such as solar or wind, because it's a 24/7 continuous process," Lovley explains. "And it will work in just about any environment on earth."

He suggests nanowires, instead of batteries, could power some devices. "Already we can use the protein nanowires [to produce power] for small-scale electronics, like a wearable patch for medical monitoring," he says, adding that nanowires can function in living tissue without triggering a bad reaction and are more biodegradable than metals.

Lovley says companies have expressed

interest in such applications. But some scientists are skeptical about separating nanowires from the bacteria that generate them. "Taking proteins that have electrical properties out of their natural context they [then] have to compete with synthetic materials" for efficiency, explains Sarah Glaven, a U.S. Naval Research Laboratory biologist. Nanowires would "be hardpressed to compete with something like a conductive metal." She has previously worked with Lovley but is not involved in his current research, instead focusing on genetically modifying conductive bacteria for applications such as marine sensors.

Given notes that nanowires would have an advantage in environments such as the ocean or human body, which corrode traditional electronics. But even in that setting, she says, nanowires would still vie with materials such as biocompatible polymers. She prefers working with living microbes because "you don't just have an electron-carrying material—you have the whole information-processing suite within the cell itself."

Although researchers are already finding applications for both living cells and harvested nanowires—and have even explored modifying the prolific bacterium *Escherichia coli* to produce pili—questions remain about which proteins make up the most productive nanowires. Understanding whether pili or another type of nanowire carries most of *Geobacter*'s electricity could guide scientists choosing the best material for electronics.

"Everybody, including us, thought [the key nanowires] were pili," says Nikhil Malvankar, a biophysicist who previously worked with Lovley but currently has his own laboratory at Yale University. Last year, however, Malvankar and his colleagues imaged Geobacter with an electron microscope; they concluded that rather than stringlike pilin proteins, stacks of proteins called cytochromes form the microbes' main electricity-transmission method. The researchers went on to examine a biofilm of the bacteria via genetic-modification experiments, as well as several imaging methods—Glaven says they "really threw the kitchen sink" at getting an accurate picture of the nanowires Geobacter was using. The Yale team pinpointed a specific hyperefficient conductor cytochrome called OmcZ, which Geobacter produces in response to an electrical field, as the biofilm's primary method of shedding electrons. "Seeing is believing, so I think microscope imaging is very important," says co-author and Yale physicist Sibel Yalcin.

But researchers still do not agree on which nanowire is most significant. Some come down on the side of pili, others for

PHYSICS

Chilling Mystery

Lasers slow molecules for a glimpse of the quantum world

Because humans are large and warm, we can rarely see quantum mechanics in action. To do so, physicists use lasers to cool atoms to just a trillionth of a degree above absolute zero. This slows the atoms' movement enough to watch them follow quantum physics rules. But cooling molecules made of more than one atom has proved more difficult: somehow these ultracold molecules tend to sneakily heat up again, so researchers can no longer keep track of them—a phenomenon physicists call "ultracold molecule loss." A study published in *Nature Physics* reveals how it happens. Being able to better see and control ultracold molecules would help scientists assemble a <u>quantum machine</u> piece by piece, says Jun Ye, a physicist at the University of Colorado Boulder, who was not involved in the study. But molecule heating throws a wrench in this process. A pioneer of <u>ultracold mole-</u> <u>cule experiments</u>, Ye observed early on that reactions—a matter of quantum chemistry instead of quantum physics were somehow heating molecules up.

Yu Liu, a researcher at Harvard University and co-leader of the study, says the researchers had planned to investigate the reactions themselves. But, Liu says, "what we saw during the process turns out to give the answer to this question" of ultracold molecule loss. The scientists slowed down the chemical reactions between molecules enough to observe their behavior while in a state called "the complex," which occurs in the middle of the reaction—before the mol-



ecules fully transform into the reaction's products. Because molecules interact with light through electrical forces, the team used lasers to keep them from flying away.

At room temperature the complex exists too briefly to observe. At low temperatures it sticks around longer, but the researchers found that this longevity has a cost: it gives the ultracold complex time to cytochromes. Lovley is firmly in the pili camp: he says that when his team (which at the time included Malvankar) genetically modified *Geobacter* so it could not produce a certain type of cytochrome, it formed biofilms that were actually more conductive than those produced by unmodified bacteria. Glaven says her own lab found that electricity moves in a *Geobacter* biofilm "overwhelmingly" through cytochromes. But she notes that yet another lab, at Michigan State University, is doing work based on Lovley's pili hypothesis.

Based on his most recent research, Malvankar favors cytochromes—but he has not ruled out a role for pili. "All the filaments we found [when bacteria were actively conducting electricity] were cytochromes," he says. "But is it possible that maybe under some conditions, it could be making pili? That's actually an open question."

The drive to figure out *Geobacter*'s conductive proteins could help researchers develop more efficient living electronics. And even without complete knowledge of conductive microbes' mysteries, bacteria-based electronic devices may soon be possible. It is still early, Lovley says, "but so far everything's been working out. I've had amazing colleagues who just know how to do things with electronic materials. Every couple of weeks they come up with something new." —*Sophie Bushwick*

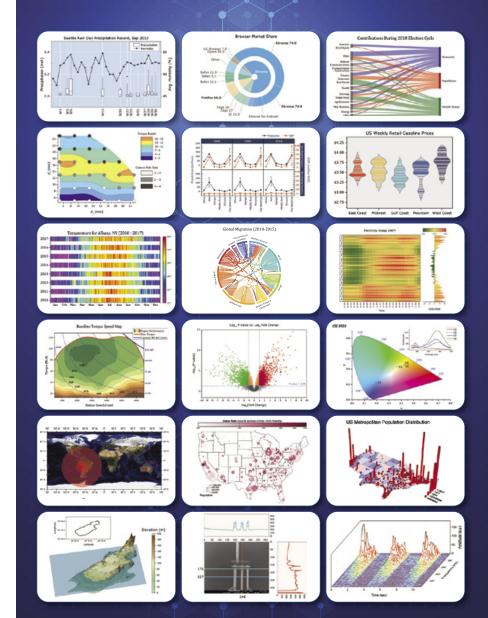
interact with the laser light keeping it in place. This interaction heats up the molecules, causing some to lose their ultracold status.

Knowing about this interaction, physicists can now avoid types of lasers that excite the complex. And the ability to see the light-complex interaction is itself promising. Nandini Mukherjee, a Stanford University chemist, who was not involved in the study, says probing the complex is a "long-sought goal in studying reaction mechanisms."

Liu says the team wants to use laser light to fully control such reactions, and co-lead author Ming-Guang Hu (also at Harvard) adds that this process could eventually illuminate how the rules of quantum mechanics make ultracold molecular reactions different from those at room temperature. Having solved a mystery that has long troubled quantum physicists, they now want to explain a lot more about quantum chemistry. —*Karmela Padavic-Callaghan*

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ADVANCES

ENVIRONMENT

Chernobyl's Legacy

Evidence builds that animals are scarcer in more heavily contaminated areas

More than 30 years after the Chernobyl nuclear plant's meltdown, an 18-mile radius around the site remains almost entirely devoid of human activity—<u>creating a haven</u> for wildlife. But scientists disagree over lingering radiation's effects on animal populations in this region, called the Exclusion Zone. A new analysis, based on estimating the actual doses animals receive in various parts of the zone, supports the hypothesis that areas with the most radiation have the fewest mammals.

"The effects we saw are consistent with conventional wisdom about radiation," says University of South Carolina biologist Timothy Mousseau, co-author of the new study in <u>Scientific Reports.</u> "What's surprising is that it

A fox pauses in the Chernobyl Exclusion Zone.

took this long to start looking at this in a rigorous, comprehensive way."

The paper reanalyzed data collected in 2009. At that time the same researchers used snow tracks to estimate the abundance of 12 mammal species, from mice to horses to wild boars, at 161 sites across 300 square miles in the Exclusion Zone. They found fewer mammals in areas with higher background radiation. Two subsequent studies, however, found no significant correlation between radiation levels and mammal abundance. But Mousseau and his colleagues say all three studies analyzed radiation exposure too simplistically.

The previous studies relied solely on measurements of ambient radiation. For their reanalysis, the researchers used their original mammal counts—but they estimated the total radiation doses those animals would likely receive over their lifetimes, combining data about each species (including range size, diet and life span) with radiation levels based on soil samples and calculations about how the animals encounter radioactive molecules.

Again, they found that locations calculated as more radioactive had fewer mammals. Many past studies have linked radia-





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tion exposure at those estimated levels to deleterious genetic, physiological and reproductive effects, Mousseau says.

"This work is very important and is well done," says Carmel Mothersill, a radiobiologist at McMaster University in Ontario, who was not involved in the study. "My own lab has used this approach to reanalyze data from <u>Fukushima</u> as well as Chernobyl, and it gives a much more meaningful relation between radiation exposure and risk of harm."

But according to University of Georgia wildlife ecologist James Beasley, a co-author of past conflicting studies, the paper suffers from "critical flaws"—primarily in how the authors estimated animal abundance. Their original measurement locations, he says, were not spaced appropriately or extensively enough to draw conclusions about the entire area.

Karine Beaugelin-Seiller, study lead author and a radioecologist at the Institute for Radiological Protection and Nuclear Safety in France, agrees that uncertainty remains. Yet, she says, the study provides a more accurate way to establish the connection between radiation exposure and effects, ideally guiding future research. —*Rachel Nuwer*



Bird Battles

Scientists have company watching woodpecker combat

The Americas' western oak woodlands are fragmented into fiercely contested territories by cadres of acorn woodpeckers, each guarding "granary" oaks storing thousands of acorns. The birds nest in groups that cooperatively raise chicks; when one member of a breeding pair in a granary-rich turf dies, rival teams of nonbreeding birds swoop in from surrounding areas to fight for the spot. These sometimes deadly struggles can last for days. Scientists have studied the skirmishes for over 50 years—but they only recently learned that other woodpeckers are keenly observing the battles, too.

Smithsonian biologist Sahas Barve led a study of these fights that was published in *Current Biology*. His group discovered the spectators by fitting dozens of birds with ultralight solar-powered radio trackers. "Power struggles are so chaotic that you can't [visually] track the movements of any one animal," Barve says.

Biologists have seen news of a breeding opportunity travel with astonishing speed. "Because animals don't have language, we often assume it's harder for them to transmit information," says Princeton University evolutionary biologist Christina Riehl, who was not involved in the study. "They're not posting about it on Facebook or talking about it in the streets." Nobody yet knows how birds in surrounding territories find out so quickly, sometimes triggering battles in minutes.

Barve's group saw that combat draws not only fighters but also birds that come to watch for up to an hour. These viewers leave their own granaries undefended, which suggests intelligence gained about rival groups is worth the risk, Riehl says.

Monitoring the relationships between individuals in other groups is rarely seen among birds, Barve says. The study shows that the woodpeckers "have a very high-level understanding of social dynamics in their population," he adds. "It highlights how much we don't know about how animals perceive and navigate a complicated social system." —*Jim Daley*



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<u>ADVANCES</u>

ASTRONOMY

Fast Radio Bursts Grow Up

The study of a strange new phenomenon goes mainstream

New subfields in astronomy tend to follow a particular sequence: Something new is observed. Researchers scratch their heads, then look for more examples of it. At first, each discovery in the new category—say, an exoplanet or gravitational-wave event generates excitement. Eventually they begin to feel routine. But that is when the science gets interesting: with enough examples, patterns emerge, and inaccurate hypotheses are weeded out.

In 2020 the study of fast radio bursts (FRBs) has crested to that point. For nearly two decades radio telescopes have been detecting these distinctive pinpoints of radio light. They come from distant galaxies and last just a fraction of a second, typically never to reappear. With hundreds of FRBs now recorded, researchers have enough data points to begin drawing conclusions about the universe.

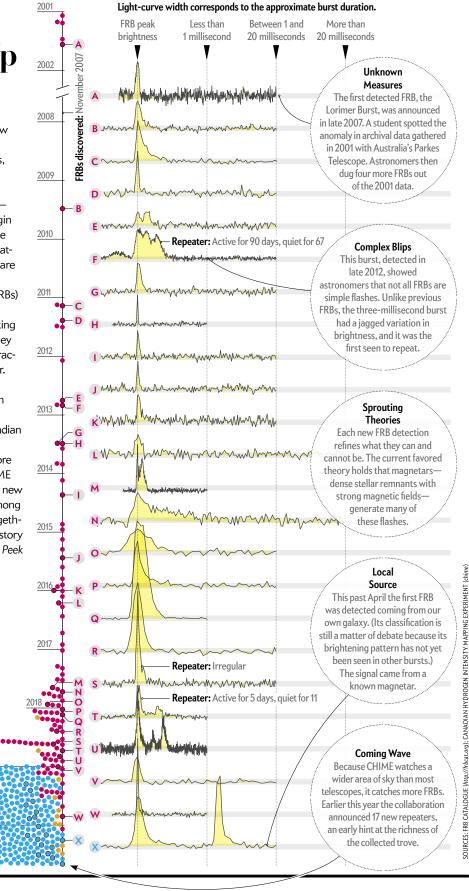
One big player in the search is the Canadian Hydrogen Intensity Mapping Experiment (CHIME), a telescope that has detected more than 700 FRBs since the start of 2019. CHIME researcher Cherry Ng says that with all the new results coming in and with coordination among astronomers growing, "we can all work together to figure out what these are." Here's the story of this field so far. —*Katie Peek*

FRB Detections

Dots mark the dates of more than 800 fast radio bursts (FRBs) detected as of September 2020. Two dozen light-curve examples appear in yellow.

- Confirmed (118)
- Unconfirmed CHIME detections (700+)
- Unconfirmed detections from other telescopes (11)

The FRBs from CHIME (*blue dots*)—whose dates are not yet published—are placed evenly across 2019 and 2020 to approximate their distribution.



SEISMOLOGY Earthquake Sounds

Natural vibrations could let scientists measure ocean warming

Sound may offer a creative way to take the ocean's temperature. Climate change is steadily <u>warming the seas</u>, which have absorbed about 90 percent of the excess heat trapped by greenhouse gases. This warming contributes to sea-level rise, imperils marine species and influences weather patterns.

But tracking the warming is tricky. Ship-based observations capture only snapshots in time over a tiny portion of the water. Satellite observations cannot penetrate very deep below the surface. The most detailed picture of ocean heat comes from <u>Argo, a flotilla of autonomous probes</u> that have peppered the seas for more than a decade and can drop down to around 6,500 feet. But there are only about 4,000 such floats, and they cannot sample deeper parts of the oceans.

In Science, researchers at the California Institute of Technology and the Chinese Academy of Sciences compared the travel speeds of sounds produced by undersea earthquakes to detect ocean warming over wider areas. Because sound travels faster in warmer water, differences in speed can reveal changing temperatures. "They're opening up a whole new area of study," says Princeton University geophysicist Frederik Simons, who was not involved in the research.

Oceanographers proposed measuring ocean heat with sound in 1979, but sea-

based acoustic emitters were expensive and raised concerns about disturbing marine animals. Inspired by those early efforts, Caltech researcher Wenbo Wu thought to monitor <u>low-frequency acoustic</u> <u>waves</u> emitted by earthquakes below the seafloor. "I know these earthquakes are very powerful sources," Wu says. "So why not try to use the earthquakes?"

He and his team tested the idea near Indonesia's island of Nias. where the Indo-Australian Plate is bumping under the Sunda Plate. The researchers gathered acoustic data from 4,272 earthquakes of magnitude 3 or greater from 2004 to 2016, and they compared acoustic wave speeds from quakes that originated in the same spot over the years. By modeling the differences, often just fractions of a second, they found that the ocean near Nias was warming by about 0.08 degree Fahrenheit per decade—more than the 0.047 degree F suggested by Argo's data. Less than one degree F does not sound large, but it takes considerable heat to warm the entire eastern Indian Ocean.

The new acoustic method is promising, says University of Hawaii oceanographer Bruce Howe, who was not involved in the work. Researchers may even be able to get a longer ocean-temperature history from seismological data taken decades ago, although older seismometers did not record the sound waves' timing as precisely as cur-

rent GPS-based ones do.

Simons and his colleagues are exploring an alternative technique, deploying dozens of underwater microphones called hydrophones to catch more earthquake sounds. He notes that pinpointing the floats' precise locations will be challenging, however. Overcoming such challenges would fill in important gaps, Wu says: "We really need different methods of [gathering] the data as much as possible." -Stephanie Pappas

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<u>ADVANCES</u>

IN THE NEWS Quick Hits By Sarah Lewin Frasier

U.S.

Western Joshua trees will get a year of temporary endangered species status in California while the state considers permanently listing the distinctive succulents as the first-ever plant species protected because of climate change-related threat.

PANAMA

A tropical forest ground survey revealed that one lightning strike often damages more than 20 trees, a quarter of which can die within a year. Researchers combined this finding with satellite data to estimate that lightning kills 200 million tropical trees worldwide every year—a significant cause of their demise.

For more details, visit www.ScientificAmerican.com/dec2020/advances

SYNTHETIC BIOLOGY

DNA Glow

Bacterial machinery unlocks new water-pollution test

Pollution from industry, agricultural runoff, pharmaceuticals and other sources contaminates water around the world, and <u>detecting it</u> can be expensive and time-consuming. Now researchers have developed a quick, potentially inexpensive way to test for at least 16 dangerous contaminants, including lead, copper and antibiotics, according to a study published in *Nature Biotechnology*.

The test takes cues from bacteria, which are especially adept at reacting to specific contaminants. "Nature has been solving this problem for billions of years," says study coauthor Julius Lucks, a chemical and biological engineer at Northwestern University. His team searched the literature to find out which proteins bacteria produce to deal with various pollutants. The researchers' new, handheld testing device takes advantage of these proteins' reactions using a series of vials: each has a freeze-dried solution that incorporates a specific protein,

GREENLAND

Climate researchers discovered records of an automatic weather station that measured -93.3 degrees Fahrenheit one day in December 1991—a temperature colder than the average on Mars and the coldest ever recorded in the Northern Hemisphere.

CHINA

Newly discovered and pristinely preserved fossils suggest two sleeping dinosaurs were buried alive in an underground burrow 125 million years ago. The burrow may have collapsed under volcanic debris.

AUSTRALIA

A new study <u>shows</u> how Australian grasslands' strange barren patches—called fairy circles—are landscaped by the grasses themselves. Baking heat creates a hard clay crust over a patch of ground; water runs off of it, forming a more welcoming zone at its edges that grasses bolster as they grow and cool the soil.

ITALY -

Scientists have examined a shark found south of Sardinia that somehow survived to three years old without skin or teeth. They concluded it was a genetic mutation and plan to check nearby sediment for potential pollutant causes.

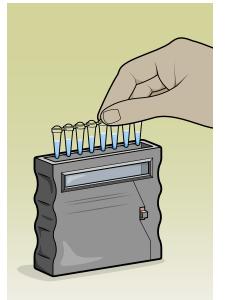
> Testers add a drop of water to each vial; when viewed in the device, vials glow when the water has their assigned contaminants.

> rescent glow if activated. The solutions also contain RNA polymerase, which makes RNA by following a DNA strand. If the protein bound to the DNA encounters its corresponding contaminant, the protein changes shape and falls off. This lets the RNA polymerase travel all the way along the DNA strand, making the sample fluoresce green.

> The study is "a really nice, clever and creative use of synthetic biology and highlights what the field can do well," says Mary Dunlop, a synthetic biologist at Boston University, who was not involved in the research.

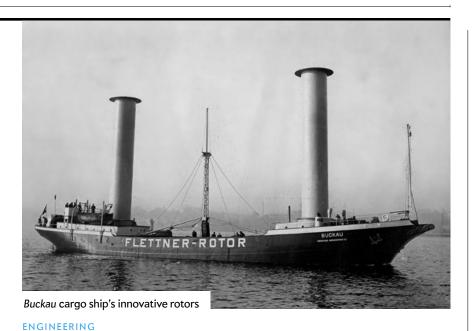
> Researchers have used a similar method to detect pathogens, but this device is the first to identify so many pollutants, Lucks says. The test is "very promising," says Susan Richardson, a University of South Carolina chemist, who focuses on water issues and was not involved in the research. She cautions, however, that it may need to react to lower contaminant concentrations before it can be widely useful.

—Susan Cosier



which causes the mixture to glow green when an added drop of water contains a particular contaminant.

Each solution includes custom-engineered strands of DNA with one section that a pollutant-sensing protein is bound to and another section that generates a fluo-



Rotating Sails

A century-old concept gets a fresh look as shippers cut back on fuel

In 1926 a cargo ship called the Buckau crossed the Atlantic sporting what looked like two tall smokestacks. But these towering cylinders were actually drawing power from the wind. Called Flettner rotors, they were a surprising new invention by German engineer Anton Flettner (covered at the time in Scientific American). When the wind was perpendicular to the ship's course, a motor spun the cylinders so their forwardfacing sides turned in the same direction as the wind; this movement made air move faster across the front surface and slower behind, creating a pressure difference and pulling the ship forward. The rotating sails provided a net energy gain-but before they could be widely adopted the Great Depression struck, followed by World War II. Like the electric car, the Flettner rotor would be abandoned for almost a century in favor of burning fossil fuel.

Now, with shippers under renewed pressure to cut both costs and carbon emissions, the concept is getting another shot. In one notable example, the 12,000-gross-ton cargo vessel *SC Connector* is adding 35-meter Flettner rotors that can tilt to near horizontal when the ship passes under bridges or power lines. The new rotors need electrical power to spin, but manufacturer Norsepower says they can still save up to 20 percent on fuel consumption and cut emissions by 25 percent. The *SC Connector* is one of a growing series of rotor-boosted ships expected to be operating in various parts of the world by year's end, according to SSPA, a Sweden-based nonprofit research institute. Shipbuilders are also incorporating other wind-propulsion technologies, such as kite-style sails. But Flettner rotors are getting the earliest adoption, says Sofia Werner, a naval architect who leads an SSPA team studying their performance. Ships can easily be retrofitted, literally overnight, with rotors activated by an on/off switch. "It's a quite simple solution, understandable and safe," Werner says. "It's also very visible, which is good for marketing."

The United Nations International Maritime Organization has set ambitious decarbonization goals involving marine fuels, and the European Union is now funding rotor research. Climate pressures and easy installation make wind-power systems an attractive option, according to the International Windship Association. "A lot of people wanted to see wind dead [in the 1920s] because they were making a lot of money off fuel," says Gavin Allwright, the organization's secretary-general. "That's still true today. I can't sell you a unit of wind. What I am bullish about is that where we've got a major decarbonization issue, [alternative fuels] have great potential but are five to 10 years from being proven out. Wind, we could put on a vessel today."

—Lynn Freehill-Maye

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Wyatt Townley is Poet Laureate of Kansas Emerita. Her work has been read on NPR, featured in American Life in Poetry, and published in journals, among them *North American Review*, the *Paris Review* and the Yale Review. Her latest book of poems is *Rewriting the Body* (Stephen F. Austin State University Press, 2018).



Staring at Nothing

-for Dr. Robert Williams, astronomer

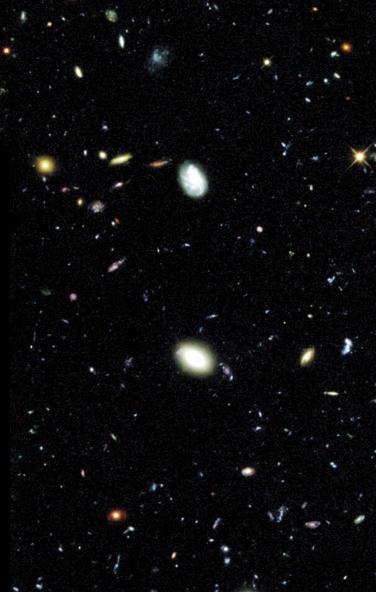
What are you staring at? said the mother, said the cousin, said the teacher to the child— Nothing, he said. Then his wife asked. Nothing.

Nothing and more nothing and nothing more. What a *waste of time*, said his colleagues, valuable time. People would kill for that.

One December for ten nights and a hundred hours, he stared at nothing. He looked at where there wasn't anything but nothing, more nothing,

and nothing more. Nothing but death and birth merging into light—collisions of blue, red, yellow, white. Spirals, ellipticals, nothing

but the universe quintupling in size. What wasn't is teeming with galaxies, gleaming innumerably. It's nothing, said he. Look at nothing to see.



AUTHOR'S NOTE: In December 1995 astronomer Robert Williams took a risk that was mocked by his colleagues at the Space Telescope Science Institute. As director, Williams used his discretionary time with the Hubble Space Telescope to point at nothing—an apparently empty spot of sky—over a 10-day period. The astounding revelation of thousands of galaxies is now known as the legendary Hubble Deep Field.



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.



The Mental Toll of COVID-19

The rise in depression and anxiety is even worse than expected, especially among young adults

By Claudia Wallis

You didn't need a crystal ball to forecast that the COVID-19 pandemic would devastate mental health. Illness or fear of illness, social isolation, economic insecurity, disruption of routine and loss of loved ones are known risk factors for depression and anxiety. Now studies have confirmed the predictions. But psychologists say the findings also include surprises about the wide extent of mental distress; the way media consumption exacerbates it; and how badly it has affected young people.

For example, a report from the U.S. Centers for Disease Control and Prevention, published in August, found a tripling of anxiety symptoms and a quadrupling of depression among 5,470 adults surveyed compared with a 2019 sample. Similarly, two nationally representative surveys conducted in April, <u>one by</u> researchers at the Boston University School of Public Health and another at Johns Hopkins University, found that the prevalence of depressive symptoms (B.U.) and "serious psychological distress" (Hopkins) were triple the level measured in 2018. "These rates were higher than what we've seen after other largescale traumas like September 11th, Hurricane Katrina and the Hong Kong unrest," says Cath-

erine Ettman, lead author of the B.U. study. Some of the most affected groups in

these studies were people who had preexisting mental health issues, low-income individuals, people of color, and those close to someone who suffered or died from COVID-19. In Ettman's study, however, the group in the U.S. with the single biggest rise in depression—up fivefold—was of Asian ethnicity. In an accompanying <u>commentary</u>, psychiatrist Ruth Shim suggested the upsurge could reflect the impact of racism and slurs related to the pandemic's origin in China.

An unanticipated finding, across all three surveys, was the outsized toll on young adults. In the CDC survey, 62.9 percent of 18- to 24-year-olds reported an anxiety or depressive disorder, a quarter said they were using more drugs and alcohol to cope with pandemic-related stress, and a quarter said they had "seriously considered suicide" in the previous 30 days. Young adults were also the most affected age group in an <u>unusual</u>, real-time study that tracked the rapid rise in "acute distress" and depression at three points between mid-March and mid-April. "We expected the opposite because it was already clear that older individuals were at greater risk" from the virus, says senior author Roxane Cohen Silver, a psychologist at the University of California, Irvine.

Silver suspects that young people "may have had more disruption in life events: graduations, weddings, the senior year of college and of high school. All those transitions were disrupted, as well as school and social connections, which we know are very important for young people."

Her study, which involved 6,500 people, does point to one major contributor to anxiety for people of all ages: increased engagement with media coverage of the outbreak. Especially problematic is exposure to conflicting information. Silver, who has studied the psychological fallout of events such as 9/11 and the 2013 Boston Marathon bombing, says that a fixation on media coverage is a known risk factor: "If people are engaged with a great deal of media, they are more likely to exhibit and report distress, but that distress seems to draw them further into the media. It's a cyclical pattern from which it is difficult to extricate oneself."

Silver and others who investigate mass trauma have suggestions for keeping mental equilibrium in challenging times. Limiting media consumption and avoiding sensationalist reports is one. Maintaining social contacts—via Zoom, phone or other COVID-safe methods—is also vital, says psychologist James Pennebaker of

> the University of Texas at Austin. "Unlike any other disaster that I've studied, people are actively less close to friends and community," says Pennebaker, who is examining the pandemic's mental health impact by analyzing posts on the social media platform Reddit.

Fewer hugs and less shared grieving may help explain why people do not seem to be adjusting to the new normal, Pennebaker says. "This is not 9/11 or an earthquake, where something big happens, and we all get back to normal pretty quickly." His other tips are to maintain healthy sleep, exercise, food and drink habits. Keep a journal, too. Research shows that expressive writing helps people process difficult emotions and find

meaning, he says: "If you're worrying about COVID too much, try writing about it."



ASTRONOMY EXPLOSIONS AT THE EDUCATION OF THE STRONOMY

Most stars die in fairly predictable ways, but astronomers have discovered a growing number of unusual supernovae that challenge the traditional picture

> By Anna Y. Q. Ho Illustration by Kenn Brown, Mondolithic Studios

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Anna Y. Q. Ho is a Miller Fellow in the astronomy department at the University of California, Berkeley. She studies the catastrophic deaths of massive stars.



N SEPTEMBER 9, 2018, A ROBOTIC TELESCOPE ON ITS ROUTINE PATROL OF THE night sky detected what looked like a new star. Over the next few hours, the "star" grew 10 times brighter, triggering a flag by software I had written to identify unusual celestial events. It was night-time in California, and I was asleep, but my colleagues on the other side of the world reacted quickly to the alert. Twelve hours later we had obtained enough additional data from telescopes on Earth

and in space to confirm that this was the explosion of a star—a supernova—in a distant galaxy. But this was no ordinary supernova.

Tying together the evidence from different telescopes, we concluded that after shining for millions of years, the star did something surprising and mysterious: it abruptly cast off layers of gas from its surface, forming a cocoon around itself. A few days or a week later the star exploded. The debris from the blast collided with the cocoon, producing an unusually bright and short-lived flash of light. Because the explosion took place in a galaxy far away—the light took almost a billion years to reach Earth—it was too dim to be seen with the naked eye but bright enough for our observatories. Through a retrospective search of telescope data, we were even able to detect the star in the act of shedding two weeks before it exploded, when it was one one-hundredth as bright as the explosion itself.

This was just one of several recent discoveries that have shown us that <u>stars die in surprisingly diverse</u> ways. Sometimes, for example, the remnant of a star's core that is left over after a supernova remains active after the star has collapsed—it can launch a jet of material moving at hyperrelativistic speeds, and the jet itself can destroy the star with more energy than a normal supernova. Sometimes, in the final days to years of its life, a star blows away a significant fraction of its gas in a series of violent eruptions. These extreme deaths appear to be rare, but the fact that they happen at all tells us there is much we still do not understand about the basics of how stars live and die.

Now my colleagues and I are amassing a collection of unusual stellar endings that challenge our traditional assumptions. We are beginning to be able to ask and answer fundamental questions: Which factors determine how a star dies? Why do some <u>stars end</u> their lives with eruptions or violent jets, while others simply explode?

A NEW STAR

THE STORY OF STELLAR BIRTH, life and death is a tale of competing forces. Stars are formed in interstellar clouds of hydrogen gas when the force of gravity pulls part of the cloud inward strongly enough to overcome the outward push of magnetic fields and gas particles traveling at high speeds. As the cloud fragment collapses, it becomes 20 orders of magnitude denser and heats up by millions of degrees—temperatures high enough for the hydrogen atoms to collide and stick together to form helium. Fusion has begun, and a new star is born.

Like a cloud, a star is itself a battleground, with gravity pushing in and pressure from nuclear fusion pushing out. The evolution of a star depends on its temperature, which in turn depends on its mass. The heavier the star, the heavier the elements it can forge, and the faster it burns through its fuel. The lightest stars fuse hydrogen to helium and stop there—the sun is more than four billion years old and is still burning its hydrogen. Heavier stars live much shorter lives, only 10 million years or so, yet manufacture a much longer chain of elements: oxygen, carbon, neon, nitrogen, magnesium, silicon and even iron.

A star's mass also determines how it will die. Lightweight stars—those that weigh less than around eight times the mass of the sun—die relatively peacefully. After exhausting their supplies of nuclear fuel, the outer layers of these stars blow out into space, forming beautiful planetary nebulae and leaving the stars' cores exposed as white dwarfs—hot, dense objects with about half the mass of the sun that are only slightly larger than Earth.

Heavier stars, however, meet a violent end because of the enormous temperatures and pressures in their cores. Around the time they reach iron in the nuclear burning chain, conditions are so hot that things fall apart-iron atoms can start breaking into smaller pieces. The chain of fusion is cut off, and the star loses its internal pressure. Gravity takes over, and the core collapses until its constituent atoms are so close together that another opposing force steps in: the strong nuclear force. Now the core has become a neutron star, an exotic and dense state of matter made mostly of neutrons. If the star is massive enough-say, more than 20 times the mass of the sun-gravity overcomes even the strong nuclear force, and the neutron star collapses further into a black hole. Either way, some of the energy released when the core collapses pushes the outer layers of the star into space, creating an explosion so bright that for a few days it outshines the rest of the stars in the galaxy combined.

Human beings have spotted supernovae by eye for thousands of years. In 1572 a Danish astronomer named Tycho Brahe noticed a new star in the constellation Cassiopeia. It was as bright as Venus and stayed that bright for months before fading away. He wrote that he was so shocked that he doubted his own eyes. Today the aftermath of the explosion—the debris—is still visible and is known as Tycho's Supernova Remnant.

For a supernova to be bright enough to be seen by the unaided eye, it must be in the Milky Way, as Tycho's supernova was, or in one of its satellite galaxies, and this is rare. I might not see a supernova without the help of a telescope in my lifetime, although I can hope. In the past century astronomers began using telescopes to find supernovae beyond the Milky Way by taking repeated observations of the same set of galaxies and looking for changes, called transients. Our telescopes are now roboticized and outfitted with modern cameras, enabling us to discover thousands of supernovae every year.

An early sign that some stars die in extreme ways was the 1960s discovery of <u>gamma-ray bursts</u> (GRBs), so named because of the bright blasts of gamma-ray light they emit. We believe we see them when a massive star collapses into a neutron star or a black hole, the newborn compact object launches a narrow jet of matter, that jet successfully tunnels from the core through what remains of the star, *and* the jet just happens to be pointing at Earth.

What might create such a jet? The basic idea is the following. When a normal star runs out of fuel and dies, its core collapses into a neutron star or a black hole, and that is the end of that. In a gamma-ray burst, however, the corpse stays active. Perhaps the nascent black hole is absorbing mass from a disk of material around it, releasing energy in the process. Or maybe the newly created neutron star is rotating quickly, and a powerful magnetic field acts as a brake, releasing energy as the star slows down. Either way, this "central engine" pumps out energy that gets funneled into a jet of extremely hot plasma that tunnels from the center of the star out through the infalling material, glowing in gamma rays.

The passage of the jet through the star causes it to explode in a special supernova dubbed "Type Ic-BL," which is 10 times more energetic than ordinary supernovae. As the jet plows into the surrounding gas and dust, it produces light all across the electromagnetic spectrum, called an afterglow. Afterglows are difficult to find because although they are 1,000 times brighter than typical supernovae, they are 100 times more fleeting, appearing and disappearing in just a few hours. The best hope for finding an afterglow is to wait for a gamma-ray burst to be discovered by a satellite and then immediately point your telescope to the reported location of the burst.

By waiting for a satellite to discover a burst, though, you limit the kinds of phenomena you can discover. A lot of things have to go right for a GRB to be produced: the jet has to be launched, make it through the star, and be pointing at you. In fact, it seems extremely unlikely for GRBs to occur: the gamma-ray photons emitted by the jet should get trapped unless the jet is moving at 99.995 percent of the speed of light. But to reach such speeds, the jet would need to somehow make it through the star without dragging along the star's matter with it. What if most jets actually do get slowed down by the star, and we see only the small fraction that make it through unscathed? In other words, perhaps gamma-ray bursts represent the rare occasions that jets escape their stars and don't slow down too much. If that were true, there would be a huge number of extreme stellar deaths out there that are totally invisible to gamma-ray satellites.

For my thesis, I set out to find afterglows without

Surprising Supernovae

For a long time the story of stellar death was simple: the life and fate of a star were thought to depend almost exclusively on its mass **A**. But discoveries of strange supernovae in the past decade, and especially the past few years, have shown that the story is much more complicated than that. Sometimes the core of a dying star becomes an engine that launches a powerful jet or a wind that explodes the star with extra energy **B**. Other times stars cast off material before they die, exhibiting death omens that foretell the coming explosion **G**.

A CLASSIC MODEL

Traditionally a star's mass was thought to dictate its death. Different types of supernova explosions should occur for different ranges of stellar mass, leading to various remnant end products. Although this story is still largely true, sometimes the usual process goes off the rails, and different endings ensue (shown in green, orange, blue and yellow circles).

Mass of star (relative to the sun)	Death progression	Corpse (remnant)
8-10×	Electron-capture supernova	→ Neutron star
10-20×	→ Type-II core-collapse supernova	→ Neutron star
20-40×	Type-II core-collapse supernova	→ Black hole
40-100×	► Type-Ibc core-collapse supernova	> Black hole
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100-260×	Pair-instability supernova	→ Nothing
Greater than 260×		Black hole

ODDITY: DEATH OMENS

Astronomers have found that some massive stars shed a significant portion of their atmospheres in the final days to weeks of their lives. When the star finally explodes, the debris from the blast collides with the recently shed material, producing a brilliant display. Why some stars do this and others do not is unknown. Perhaps it is the result of rapid rotation or interaction with another star? Perhaps it happens because of changes deep within the star that occur during the final stages of nuclear burning? One example, based on the recently observed supernova SN2018gep, is shown here (*circled in blue*).



Star

Superluminous supernova (neutron star launches a wind)

Neutron star with strong

magnetic field (magnetar)

AT2018cow

BODDITY: ENGINE-DRIVEN EXPLOSIONS

Sometimes it seems that the corpse of a dead star—a newly created neutron star or black hole—remains active and forms an engine that launches a powerful jet or wind. This probably happens when the star's core is rotating extremely quickly at the time of collapse. Maybe the star was spinning fast to begin with or gained speed through an interaction with a binary companion. Examples of engine-driven explosions are shown here (circled in green, orange and yellow).

Wind —

Jet

Stellar remnant/ material

Gamma-ray burst (black hole launches a fast jet) or dirty fireball (black hole launches a slow jet)

Rapidly spinning black hole

Stellar remnant material

Jets stifled inside recently shed material

Jet cocoon

Jet

A dense torus of gas and dust that presumably used to be part of the star and was recently shed

> Slow jet launched by a black hole or maybe a magnetar driving a wind

black hole

Spinning

Explosion debris hits shell

Neutron star (likely)

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relying on a trigger from a satellite. My plan was to use the Zwicky Transient Facility, a robotic telescope at the Palomar Observatory in California, to patrol the sky for unusually fleeting, unusually bright points of light—and then react quickly. When I presented my thesis proposal in May 2018, my faculty advisers warned me that I might not find what I was looking for. They urged me to keep an open mind because new avenues of inquiry might arise. One month later that is exactly what happened. And two years later when I graduated, my thesis looked very different from what I had expected.

HOLY COW

WHEN I BEGAN MY WORK, I wrote a program to find celestial phenomena that were changing in brightness more rapidly than ordinary supernovae. On a normal day I examined 10 to 100 different candidates and concluded that none of them were what I was looking for.

Extreme deaths appear to be rare, but the fact that they happen at all tells us there is much we still do not understand about the basics of how stars live and die.

On some days, though, I encountered something that gave me pause.

In June 2018 I saw a report from a robotic telescope facility called ATLAS, reporting a strange event dubbed AT2018cow. "AT" stood for "astronomical transient," the prefix automatically given to all new transients, "2018" for the year of discovery, and "cow" was a unique string of letters. In the next couple of days there were reports of similarities between this event and gamma-ray bursts, yet there had been no detected show of gamma rays. "Aha," I thought, "this is it!" Because AT2018cow was so bright and so nearby, there was <u>intense world-</u> wide interest in this object, and astronomers observed it all across the electromagnetic spectrum. I immediately made plans to observe AT2018cow using a radio telescope in Hawaii called the Submillimeter Array.

AT2018cow stunned just about everyone. It unfolded completely differently than any cosmic explosion seen before. We were like the people in a classic parable who are trying to identify an elephant in the dark. One person feels its trunk and says it is a waterspout, whereas another feels the ear and thinks it must be a fan, and a third feels the leg and says it is a tree. Similarly, AT2018cow shared characteristics with several different classes of phenomena, but it has been difficult to put a complete picture together.

My collaborators and I spent long days and nights going over our data repeatedly, trying to figure out how to interpret them. Some of those moments-calculating the properties of the shock wave together on a chalkboard, a team member running down the hallway waving a piece of paper with new results, and meeting a colleague's eyes in shock when a beautiful new measurement came in-remain my most treasured memories from graduate school. In the end, we concluded that there were two important components to AT2018cow. The first was a central engine, as in a gamma-ray burst, but lasting for much longer-weeks rather than the typical days; x-rays shining from the heart of the explosion stayed bright for much longer than expected. The second was that for some reason, when the star burst apart, it was surrounded by a cocoon of gas and dust with about one one-thousandth the mass of the sun. Our evidence for the cocoon is indirect:

> when the star exploded, we saw a flash of optical light and radio waves that seemed to indicate debris hitting a mass surrounding the star. Such cocoons have been seen in other types of explosions, but we do not know how they get there—it may be that the material is shed by the star shortly before exploding.

> If this theory is correct, it would be the first time astronomers have directly witnessed the birth of a compact object like a neutron star or a black hole; most of the time the

corpse is completely shrouded by what remains of the star. In the case of AT2018cow, we think we could actually see down to the compact object that produced all of this amazingly variable and bright x-ray emission. Still, we are left with many questions. What kind of star exploded? Was the central engine a neutron star or a black hole? Why did the star shed mass shortly before exploding? To make progress, we needed to find similar events, so my colleagues and I set out to find another AT2018cow using the Zwicky Transient Facility.

Three months later I thought we found one—the bright, fast-rising explosion of September 9, 2018. Initially it looked very similar to AT2018cow. Within a week, however, it became clear that this event was a Type Ic-BL supernova—the kind associated with gamma-ray bursts. Its name was SN2018gep. I was excited. Sure, it was not another AT2018cow, but we finally had something that looked like a gamma-ray burst. Within five days we had collected detailed observations all across the electromagnetic spectrum. We searched the data for evidence of a jet—but we found none. Instead, yet again, my collaborators and I concluded that we were seeing bright, fast-evolving optical emission from the collision of explosion debris with a cocoon of material.

This was a surprise. Although cocoons have been seen surrounding other types of stars, they are not commonly observed in the types of supernovae associated with gamma-ray bursts. Our discovery implies that more stars shed gas at the end of their lives than we thought. We know the gas was lost in the final moments of the star's life because it was so close to the star at the time of the explosion; if it had been cast off earlier, it would have had time to get farther away. That means the star lost a significant chunk of its outer atmosphere in the final days to weeks of its life, after shining for millions to tens of millions of years. It seems, then, that this shedding heralds the death of the star.

Once again, we were left with questions. How prevalent are these death omens in different types of stars? What is the physical mechanism that produces them? I realized that I had a new direction to my research now not just gamma-ray bursts and jets but also the warning signs of soon-to-explode massive stars. And perhaps these different phenomena were even connected.

It was not until the final six months of my Ph.D. program that I finally found a gamma-ray burst afterglow. On January 28, 2020, I did my usual candidate review when I saw something that looked promising. I knew better than to get excited-there had been many, many false starts over the years. I immediately requested additional observations with a telescope in La Palma in the Canary Islands, and they confirmed that this source was fading away quickly, as would be expected for an afterglow. That night I requested urgent observations on the 200-inch Hale Telescope at the Palomar Observatory that showed the source was still fading. The next night I obtained observations with the Swift X-ray space telescope and detected x-rays from the event, all but confirming this was truly a GRB afterglow. The night after that I got a brief window of time on the Keck Telescope on Mauna Kea in Hawaii, with the hope of measuring how far away the explosion was.

I slept in a sleeping bag in the remote observing room at my university, the California Institute of Technology, and set an alarm for 4 A.M. When the time came, I felt panicked-I was squeezing in this observation right at the end of the night, the sky was getting brighter quickly, the source was very faint, and I was terrified of being too late. I did the best that I could. When it was too bright to observe any longer, I called my colleague Dan Perley of Liverpool John Moores University in England on Skype, and we looked at the data together. I was lucky. The source was faint, but there was a big, booming, obvious feature in the light from the event that enabled us to measure the distance, which was vast: a redshift of 2.9, which means its light had significantly reddened during its journey through the cosmos. When this star exploded, the universe was only 2.3 billion years old. The photons from the blast took 11.4 billion years to reach Earth. Today the physical location of the burst is 21 billion light-years away-the explosion happened so long ago that the universe has expanded significantly since then. This was the real deal.

A few months after finding our first afterglow, we found a second. To put that in perspective, prior to the

Zwicky Transient Facility, only three afterglows had ever been found without a gamma-ray burst first occurring and telling astronomers where to look, and we found two in just a few months. Now that we have our search strategy ironed out and working, I hope we can find these routinely. Still, even with two afterglows in hand, I cannot definitively answer the questions I originally set out to answer. It is difficult to tell whether any given afterglow is something new or just a normal gamma-ray burst that high-energy satellites happened to miss. We will need to find more events before we can tell if we are witnessing truly different phenomena.

EXPANDING THE CATALOG

SINCE THE DISCOVERY of an unexpected new type of enginedriven explosion in AT2018cow, my search has uncovered a variety of unusual stellar displays. There was the weird Ic-BL supernova (the kind associated with GRBs) crashing into a cocoon of material but showing no evidence for a powerful jet (the hallmark of a GRB). Then there was another event similar to AT2018cow. There were also two Ic-BL supernova that probably had jets, but these were less energetic and wider than those in traditional gamma-ray bursts. And finally, right at the end of graduate school, two actual cosmological afterglows, one of which turned out to have an associated gamma-ray burst.

So far we astronomers have been like zoologists, going out into relatively uncharted territory and characterizing all the different creatures (in this case, explosions) that we see. The next stage will be to look for patterns. What are the relative rates of each type of blast? Do they seem to occur in one type of galaxy but not another? Are these different categories actually different "species" or just different manifestations of the same phenomenon?

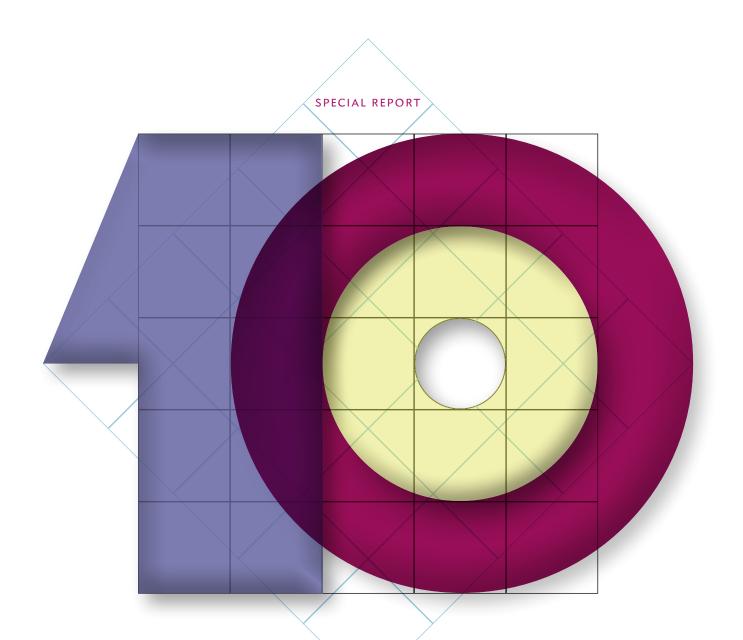
To answer these questions, we will need a much larger catalog. Beginning in a few years, the Vera C. Rubin Observatory, currently under construction in Chile, will use the largest digital camera ever constructed (three billion pixels) to spot 10 million potential transients every night-10 times more than the Zwicky Transient Facility does now. With more data, I would like to investigate which stars lose some of their mass right before they die and how often. I want to study how we can tell if there was a jet that got choked inside a star and how to recognize the kind of faint emission emitted during a star's death throes to predict where and when a star will explode. Ultimately I would like to probe questions about the factors that lead to these unusual deathsperhaps it is something about a star's rate of spin or its history of interactions with other stars that causes it to die in such a spectacular and rare way.

FROM OUR ARCHIVES

Stellar Fireworks. Daniel Kasen; June 2016.

scientificamerican.com/magazine/sa





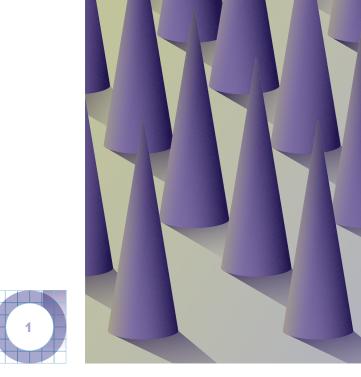
TOP 10 EMERGING TECHNOLOGIES OF 2020

Experts highlight advances with the potential to revolutionize industry, health care and society

Illustrations by Vanessa Branchi

IF SOME OF THE MANY THOUSANDS OF human volunteers needed to test coronavirus vaccines could have been replaced by digital replicasone of this year's Top 10 Emerging Technologies-COVID-19 vaccines might have been developed even faster, saving untold lives. Soon virtual clinical trials could be a reality for testing new vaccines and therapies. Other technologies on the list could reduce greenhouse gas emissions by electrifying air travel and enabling sunlight to directly power the production of industrial chemicals. With "spatial" computing, the digital and physical worlds will be integrated in ways that go beyond the feats of virtual reality. And ultrasensitive sensors that exploit quantum processes will set the stage for such applications as wearable brain scanners and vehicles that can see around corners.

These and the other emerging technologies have been singled out by an international steering group of experts. The group, convened by Scientific American and the World Economic Forum, sifted through more than 75 nominations. To win the nod, the technologies must have the potential to spur progress in societies and economies by outperforming established ways of doing things. They also need to be novel (that is, not currently in wide use) yet likely to have a major impact within the next three to five years. The steering group met (virtually) to whittle down the candidates and then closely evaluate the front-runners before making the final decisions. We hope you are as inspired by the reports that follow as we are.



MEDICINE

Microneedles for Painless Injections and Tests

Fewer trips to medical labs make care more accessible

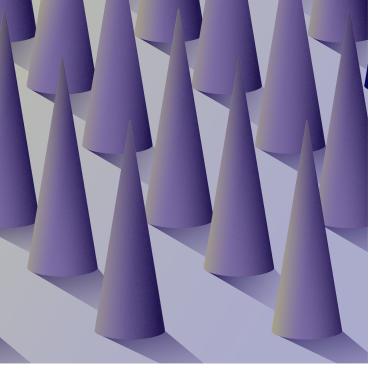
By Elizabeth O'Day

BARELY VISIBLE NEEDLES, or "microneedles," are poised to usher in an era of pain-free injections and blood testing. Whether attached to a syringe or a patch, microneedles prevent pain by avoiding contact with nerve endings. Typically 50 to 2,000 microns in length (about the depth of a sheet of paper) and one to 100 microns wide (about the width of human hair), they penetrate the dead, top layer of skin to reach into the second layer—the epidermis—consisting of viable cells and a liquid known as interstitial fluid. But most do not reach or only barely touch the underlying dermis, where the nerve endings lie, along with blood and lymph vessels and connective tissue.

Many microneedle syringe and patch applications are already available for administering vaccines, and many more are in clinical trials for use in treating diabetes, cancer and neuropathic pain. Because these devices insert drugs directly into the epidermis or dermis, they deliver medicines much more efficiently than familiar transdermal patches, which rely on diffusion through the skin. This year researchers debuted a novel technique for treating skin disorders such as psoriasis, warts and certain types of cancer: mixing star-shaped microneedles into a therapeutic cream or gel. The needles' temporary, gentle perforation of the skin enhances passage of the therapeutic agent.

Many microneedle products are moving toward commercial-

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ization for rapid, painless draws of blood or interstitial fluid and for use in diagnostic testing or health monitoring. Tiny holes made by the needles induce a local change in pressure in the epidermis or dermis that forces interstitial fluid or blood into a collection device. If the needles are coupled to biosensors, the devices can, within minutes, directly measure biological markers indicative of health or disease status, such as glucose, cholesterol, alcohol, drug by-products or immune cells.

Some products would allow the draws to be done at home and mailed to a lab or analyzed on the spot. At least one product has already cleared regulatory hurdles for such use: the U.S. and Europe recently approved the TAP blood collection device from Seventh Sense Biosystems, which enables laypeople to collect a small sample of blood on their own, whether for sending to a lab or for self-monitoring. In research settings, microneedles are also being integrated with wireless communication devices to measure a biological molecule, use the measurement to determine a proper drug dose, and then deliver that dose—an approach that could help realize the promise of personalized medicine.

Microneedle devices could enable testing and treatment to be delivered in underserved areas because they do not require costly equipment or a lot of training to administer. Micron Biomedical has developed one such easy-to-use device: a bandage-sized patch that anyone can apply. Another company called Vaxas is developing a microneedle vaccine patch that in animal and early human testing elicited enhanced immune responses using a mere fraction of the usual dose. Microneedles can also reduce the risk of transmitting blood-borne viruses and decrease hazardous waste from the disposal of conventional needles.

Tiny needles are not always an advantage; they will not suffice when large doses are needed. Not all drugs can pass through microneedles, nor can all biomarkers be sampled through them. More research is needed to understand how factors such as the age and weight of the patient, the site of injection and the delivery technique influence the effectiveness of microneedle-based technologies. Still, these painless prickers can be expected to significantly expand drug delivery and diagnostics, and new uses will arise as investigators devise ways to use them in organs beyond the skin.

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CHEMICAL ENGINEERING

Sun-Powered Chemistry

Visible light can drive processes that convert carbon dioxide into common materials

By Javier Garcia Martinez

THE MANUFACTURE of many chemicals important to human health and comfort consumes fossil fuels, thereby contributing to extractive processes, carbon dioxide emissions and climate change. A new approach employs sunlight to convert waste carbon dioxide into these needed chemicals, potentially reducing emissions in two ways: by using the unwanted gas as a raw material and sunlight, not fossil fuels, as the source of energy needed for production.

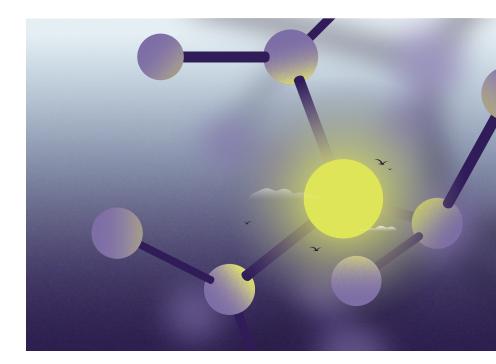
This process is becoming increasingly feasible thanks to advances in sunlight-activated catalysts,

or photocatalysts. In recent years investigators have developed photocatalysts that break the resistant double bond between carbon and oxygen in carbon dioxide. This is a critical first step in creating "solar" refineries that produce useful compounds from the waste gas including "platform" molecules that can serve as raw materials for the synthesis of such varied products as medicines, detergents, fertilizers and textiles.

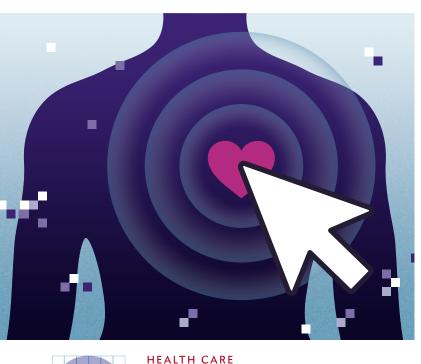
Photocatalysts are typically semiconductors, which require high-energy ultraviolet light to generate the electrons involved in the transformation of carbon dioxide. Yet ultraviolet light is both scarce (representing just 5 percent of sunlight) and harmful. The development of new catalysts that work under more abundant and benign visible light has therefore been a major objective. That demand is being addressed by careful engineering of the composition, structure and morphology of existing catalysts, such as titanium dioxide. Although it efficiently converts carbon dioxide into other molecules solely in response to ultraviolet light, doping it with nitrogen greatly lowers the energy required to do so. The altered catalyst now needs only visible light to yield widely used chemicals such as methanol, formaldehyde and formic acid—collectively important in the manufacture of adhesives, foams, plywood, cabinetry, flooring and disinfectants.

At the moment, solar chemical research is occurring mainly in academic laboratories, including at the Joint Center for Artificial Photosynthesis, run by the California Institute of Technology in partnership with Lawrence Berkeley National Laboratory; a Netherlands-based collaboration of universities, industry and research and technology organizations called the Sunrise consortium; and the department of heterogeneous reactions at the Max Planck Institute for Chemical Energy Conversion in Mülheim, Germany. Some start-ups are working on a different approach to transforming carbon dioxide into useful substances-namely, applying electricity to drive the chemical reactions. Using electricity to power the reactions would obviously be less environmentally friendly than using sunlight if the electricity were derived from fossil-fuel combustion, but reliance on photovoltaics could overcome that drawback.

The advances occurring in the sunlight-driven conversion of carbon dioxide into chemicals are sure to be commercialized and further developed by start-ups or other companies in the coming years. Then the chemical industry—by transforming what today is waste carbon dioxide into valuable products—will move a step closer to becoming part of a true, waste-free, circular economy, as well as helping to make the goal of generating negative emissions a reality.



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Virtual Patients

Replacing humans with simulations could make clinical trials faster and safer

By Daniel E. Hurtado and Sophia M. Velastegui

EVERY DAY, it seems, some new algorithm enables computers to diagnose a disease with unprecedented accuracy, renewing predictions that computers will soon replace doctors. What if computers could replace patients as well? If virtual humans could have replaced real people in some stages of a coronavirus vaccine trial, for instance, it could have sped development of a preventive tool and slowed down the pandemic. Similarly, potential vaccines that weren't likely to work could have been identified early, slashing trial costs and avoiding testing poor vaccine candidates on living volunteers. These are some of the benefits of "in silico medicine," or the testing of drugs and treatments on virtual organs or body systems to predict how a real person will respond to the therapies. For the foreseeable future, real patients will be needed in late-stage studies, but in silico trials will make it possible to conduct quick and inexpensive first assessments of safety and efficacy, drastically reducing the number of live human subjects required for experimentation.

With virtual organs, the modeling begins by feeding anatomical data drawn from noninvasive high-resolution imaging of an individual's actual organ into a complex mathematical model of the mechanisms that govern that organ's function. Algorithms running on powerful computers resolve the resulting equations and unknowns, generating a virtual organ that looks and behaves like the real thing.

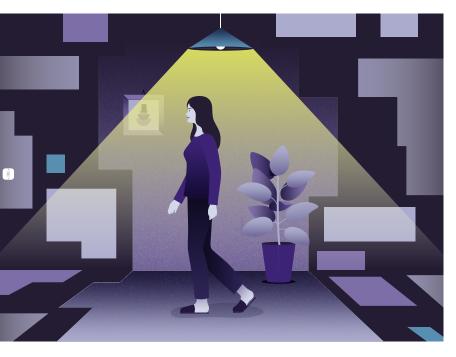
In silico clinical trials are already underway to an extent. The U.S. Food and Drug Administration, for instance, is using computer simulations in place of human trials for evaluating new mammography systems. The agency has also published guidance for designing trials of drugs and devices that include virtual patients.

Beyond speeding results and mitigating the risks of clinical trials, in silico medicine can be used in place of risky interventions that are required for diagnosing or planning treatment of certain medical conditions. For example, HeartFlow Analysis, a cloud-based service approved by the FDA, enables clinicians to identify coronary artery disease based on CT images of a patient's heart. The HeartFlow system uses these images to construct a fluid dynamic model of the blood running through the coronary blood vessels, thereby identifying abnormal conditions and their severity. Without this technology, doctors would need to perform an invasive angiogram to decide whether and how to intervene. Experimenting on digital models of individual patients can also help personalize therapy for any number of conditions and is already used in diabetes care.

The philosophy behind in silico medicine is not new. The ability to create and simulate the performance of an object under hundreds of operating conditions has been a cornerstone of engineering for decades, such as for designing electronic circuits, airplanes and buildings. Various hurdles remain to its widespread implementation in medical research and treatment.

First, the predictive power and reliability of this technology must be confirmed, and that will require several advances. Those include the generation of highquality medical databases from a large, ethnically diverse patient base that has women as well as men; refinement of mathematical models to account for the many interacting processes in the body; and further modification of artificial-intelligence methods that were developed primarily for computer-based speech and image recognition and need to be extended to provide biological insights. The scientific community and industry partners are addressing these issues through initiatives such as the Living Heart Project by Dassault Systèmes, the Virtual Physiological Human Institute for Integrative Biomedical Research and Microsoft's Healthcare NExT.

In recent years the FDA and European regulators have approved some commercial uses of computerbased diagnostics, but meeting regulatory demands requires considerable time and money. Creating demand for these tools is challenging given the complexity of the health care ecosystem. In silico medicine must be able to deliver cost-effective value for patients, clinicians and health care organizations to accelerate their adoption of the technology.





Spatial Computing

The next big thing beyond virtual and augmented reality

By Corinna E. Lathan and Geoffrey Ling

IMAGINE MARTHA, an octogenarian who lives independently and uses a wheelchair. All objects in her home are digitally catalogued; all sensors and the devices that control objects have been Internet-enabled; and a digital map of her home has been merged with the object map. As Martha moves from her bedroom to the kitchen, the lights switch on, and the ambient temperature adjusts. The chair will slow if her cat crosses her path. When she reaches the kitchen, the table moves to improve her access to the refrigerator and stove, then moves back when she is ready to eat. Later, if she begins to fall when getting into bed, her furniture shifts to protect her, and an alert goes to her son and the local monitoring station.

The "spatial computing" at the heart of this scene is the next step in the ongoing convergence of the physical and digital worlds. It does everything virtual-reality and augmented-reality apps do: digitize objects that connect via the cloud; allow sensors and motors to react to one another; and digitally represent the real world. Then it combines these capabilities with high-fidelity spatial mapping to enable a computer "coordinator" to track and control the movements and interactions of objects as a person navigates through the digital or physical world. Spatial computing will soon bring human-machine and machine-machine interactions to new levels of efficiency in many walks of life, among them industry, health care, transportation and the home. Major companies, including Microsoft and Amazon, are heavily invested in the technology.

As is true of virtual and augmented reality, spatial computing builds on the "digital twin" concept familiar from computer-aided design (CAD). In CAD, engineers create a digital representation of an object. This twin can be used variously to 3-D-print the object, design new versions of it, provide virtual training on it or join it with other digital objects to create virtual worlds. Spatial computing makes digital twins not just of objects but of people and locations-using GPS, lidar (light detection and ranging), video and other geolocation technologies to create a digital map of a room, a building or a city. Software algorithms integrate this digital map with sensor data and digital representations of objects and people to create a digital world that can be observed, quantified and manipulated and that can also manipulate the real world.

In the medical realm, consider this futuristic scenario: A paramedic team is dispatched to an apartment in a city to handle a patient who might need emergency surgery. As the system sends the patient's medical records and real-time updates to the technicians' mobile devices and to the emergency department, it also determines the fastest driving route to reach the person. Red lights hold crossing traffic, and as the ambulance pulls up, the building's entry doors open, revealing an elevator already in position. Objects move out of the way as the medics hurry in with their stretcher. As the system guides them to the ER via the quickest route, a surgical team uses spatial computing and augmented reality to map out the choreography of the entire operating room or plan a surgical path through this patient's body.

Industry has already embraced the integration of dedicated sensors, digital twins and the Internet of Things to optimize productivity and will likely be an early adopter of spatial computing. The technology can add location-based tracking to a piece of equipment or an entire factory. By donning augmented-reality headsets or viewing a projected holographic image that displays not only repair instructions but also a spatial map of the machine components, workers can be guided through and around the machine to fix it as efficiently as possible-shrinking down time and its costs. Or if a technician were engaging with a virtual-reality version of a true remote site to direct several robots as they built a factory, spatial-computing algorithms could help optimize the safety, efficiency and quality of the work by improving, for example, the coordination of the robots and the selection of tasks assigned to them. In a more common scenario, fast-food and retail companies could combine spatial computing with standard industrial engineering techniques (such as time-motion analyses) to enhance the efficient flow of work.

TOP 10 EMERGING TECHNOLOGIES OF 2020



Digital Medicine

Apps that diagnose and even treat what ails us

By P. Murali Doraiswamy

COULD THE NEXT PRESCRIPTION from your doctor be for an app? A raft of apps in use or under development can now detect or monitor mental and physical disorders autonomously or directly administer therapies. Collectively known as digital medicines, the software can both enhance traditional medical care and support patients when access to health care is limited—a need that the COVID-19 crisis has exacerbated.

Many detection aids rely on mobile devices to record such features as users' voices, locations, facial expressions, exercise, sleep and texting activity; then they apply artificial intelligence to flag the possible onset or exacerbation of a condition. Some smart watches, for instance, contain a sensor that automatically detects and alerts people to atrial fibrillation, a dangerous heart rhythm. Similar tools are in the works to screen for breathing disorders, depression, Parkinson's, Alzheimer's, autism and other conditions. These detection, or "digital phenotyping," aids will not replace a doctor any time soon but can be helpful partners in highlighting concerns that need follow-up. Detection aids can also take the form of ingestible, sensor-bearing pills, called microbioelectronic devices. Some are being developed to detect things such as cancerous DNA, gases emitted by gut microbes, stomach bleeds, body temperature and oxygen levels. The sensors relay the data to apps for recording.

The therapeutic apps are likewise designed for a

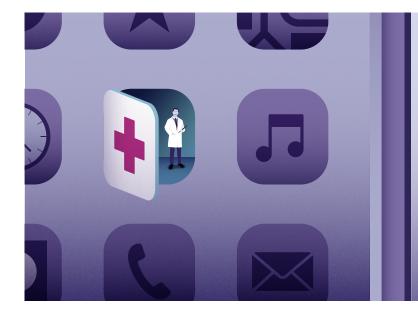
variety of disorders. The first prescription digital therapeutic to gain FDA approval was Pear Therapeutics's reSET technology for substance use disorder. Okayed in 2018 as an adjunct to care from a health professional, reSET provides 24/7 cognitive-behavioral therapy (CBT) and gives clinicians real-time data on their patients' cravings and triggers. Somryst, an insomnia therapy app, and EndeavorRX, the first therapy delivered as a video game for children with attention deficit hyperactivity disorder, received FDA clearance earlier this year.

Looking ahead, Odin, a children's health start-up, has designed a virtualreality app to treat amblyopia (lazy eye) an alternative to an eye patch. One day college students might receive alerts from a smart watch suggesting they seek help for mild depression after the watch detects changes in speech and socializing patterns; then they might turn to the Woebot chat bot for CBT counseling.

Not all wellness apps qualify as digital medicines. For the most part, those intended to diagnose or treat disorders must be proved safe and effective in clinical trials and earn regulatory approval; some may need a doctor's prescription. (In April, to help with the COVID-19 pandemic, the FDA made temporary exceptions for low-risk mental health devices.)

COVID-19 highlighted the importance of digital medicine. As the outbreak unfolded, dozens of apps for detecting depression and providing counseling became available. Additionally, hospitals and government agencies across the globe deployed variations of Microsoft's Healthcare Bot service. Instead of waiting on hold with a call center or risking a trip to the emergency room, people concerned about experiencing, say, coughing and fever could chat with a bot, which used naturallanguage processing to ask about symptoms and, based on AI analyses, could describe possible causes or begin a telemedicine session for assessment by a physician. By late April the bots had already fielded more than 200 million inquiries about COVID symptoms and treatments. Such interventions greatly reduced the strain on health systems.

Clearly, society must move into the future of digital medicine with care—ensuring that the tools undergo rigorous testing, protect privacy and integrate smoothly into doctors' workflows. With such protections in place, digital phenotyping and therapeutics could save health care costs by flagging unhealthy behaviors and helping people to make changes before diseases set in. Moreover, applying AI to the big data sets that will be generated by digital phenotyping and therapeutic apps should help to personalize patient care. The patterns that emerge will also provide researchers with novel ideas for how best to build healthier habits and prevent disease.





TRANSPORTATION Electric Aviation

Enabling air travel to decarbonize By Katherine Hamilton and Tammy Ma

IN 2019 AIR TRAVEL accounted for 2.5 percent of global carbon emissions, a number that could triple by 2050. While some airlines have started offsetting their contributions to atmospheric carbon, significant cutbacks are still needed. Electric airplanes could provide the scale of transformation required, and many companies are racing to develop them. Not only would electric propulsion motors eliminate direct carbon emissions, they could reduce fuel costs by up to 90 percent, maintenance by up to 50 percent and noise by nearly 70 percent.

Among the companies working on electric flight are Airbus, Ampaire, MagniX and Eviation. All are flight-testing aircraft meant for private, corporate or commuter trips and are seeking certification from the U.S. Federal Aviation Administration. Cape Air, one of the largest regional airlines, expects to be among the first customers, with plans to buy the Alice nine-passenger electric aircraft from Eviation. Cape Air's CEO Dan Wolf has said he is interested not only in the environmental benefits but also in potential savings on operation costs. Electric motors generally have longer life spans than the hydrocarbon-fueled engines in his current aircraft; they need an overhaul at 20,000 hours versus 2,000.

Forward-propulsion engines are not the only ones going electric. NASA'S X-57 Maxwell electric plane, under development, replaces conventional wings with shorter ones that feature a set of distributed electric propellers. On conventional jets, wings must be large enough to provide lift when a craft is traveling at a low speed, but the large surface area adds drag at higher speeds. Electric propellers increase lift during takeoff, allowing for smaller wings and overall higher efficiency.

For the foreseeable future, electric planes will be limited in how far they can travel. Today's best batteries put out far less power by weight than traditional fuels: an energy density of 250 watt-hours per kilogram versus 12,000 watt-hours per kilogram for jet fuel. The batteries required for a given flight are therefore far heavier than standard fuel and take up more space. Approximately half of all flights globally are fewer than 800 kilometers, which is expected to be within the range of battery-powered electric aircraft by 2025.

Electric aviation faces cost and regulatory hurdles, but investors, incubators, corporations and governments excited by the progress of this technology are investing significantly in its development: some \$250 million flowed to electric aviation start-ups between 2017 and 2019. Currently roughly 170 electric airplane projects are underway. Most electric airplanes are designed for private, corporate and commuter travel, but Airbus says it plans to have 100-passenger versions ready to fly by 2030.



INFRASTRUCTURE

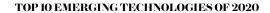
Lower-Carbon Cement

Construction material that combats climate change

By Mariette DiChristina

CONCRETE, the most widely used human-made material, shapes much of our built world. The manufacture of one of its key components, cement, creates a substantial yet underappreciated amount of human-produced carbon dioxide: up to 8 percent of the global total, according to London-based think tank Chatham House. It has been said that if cement production were a country, it would be the third-largest emitter after China and the U.S. Currently four billion tons of cement are produced every year, but because of increasing urbanization, that figure is expected to rise to five billion tons in the next 30 years, Chatham House reports. The emissions from cement production result from the fossil fuels used to generate heat for cement formation, as well as from the chemical process in a kiln that transforms limestone into clinker, which is then ground and combined with other materials to make cement.

Although the construction industry is typically resistant to change for a variety of reasons—safety and reliability among them—the pressure to decrease its contributions to climate change may well accelerate disruption. In 2018 the Global Cement and Concrete Association, which represents about 30 percent of worldwide production, announced the industry's first





Sustainability Guidelines, a set of key measurements such as emissions and water usage intended to track performance improvements and make them transparent.

Meanwhile a variety of lower-carbon approaches are being pursued, with some already in practice. Start-up Solidia in Piscataway, N.J., is employing a chemical process licensed from Rutgers University that has cut 30 percent of the carbon dioxide usually released in making cement. The recipe uses more clay, less limestone and less heat than typical processes. CarbonCure in Dartmouth, Nova Scotia, stores carbon dioxide captured from other industrial processes in concrete through mineralization rather than releasing it into the atmosphere as a by-product. Montreal-based CarbiCrete ditches the cement in concrete altogether, replacing it with a by-product of steelmaking called steel slag. And Norcem, a major producer of cement in Norway, is aiming to turn one of its factories into the world's first zero-emissions cement-making plant. The facility already uses alternative fuels from wastes and intends to add carbon capture and storage technologies to remove emissions entirely by 2030.

Additionally, researchers have been incorporating bacteria into concrete formulations to absorb carbon dioxide from the air and to improve its properties. Start-ups pursuing "living" building materials include BioMason in Raleigh, N.C., which "grows" cementlike bricks using bacteria and particles called aggregate. And in an innovation funded by DARPA and published in February in the journal *Matter*, researchers at the University of Colorado Boulder employed photosynthetic microbes called cyanobacteria to build a lower-carbon concrete. They inoculated a sandhydrogel scaffold with bacteria to create bricks with an ability to self-heal cracks.

These bricks could not replace cement and concrete in all of today's applications. They could, however, someday take the place of light-duty load-bearing materials, such as those used for pavers, facades and temporary structures.



COMPUTING

Quantum Sensing

High-precision metrology based on the peculiarities of the subatomic realm

By Carlo Ratti

QUANTUM COMPUTERS get all the hype, but quantum sensors could be equally transformative, enabling autonomous vehicles that can "see" around corners, underwater navigation systems, early-warning systems for volcanic activity and earthquakes, and portable scanners that monitor a person's brain activity during daily life.

Quantum sensors reach extreme levels of precision by exploiting the quantum nature of matter—using the difference between, for example, electrons in different energy states as a base unit. Atomic clocks illustrate this principle. The world time standard is based on the fact that electrons in cesium 133 atoms complete a specific transition 9,192,631,770 times a second; this is the oscillation that other clocks are tuned against. Other quantum sensors use atomic transitions to detect minuscule changes in motion and tiny differences in gravitational, electric and magnetic fields.

There are other ways to build a quantum sensor, however. For example, researchers at the University of Birmingham in England are working to develop free-falling, supercooled atoms to detect tiny changes in local gravity. This kind of quantum gravimeter would be capable of detecting buried pipes, cables and other objects that today can be reliably found only by digging. Seafaring ships could use similar technology to detect underwater objects.

Most quantum-sensing systems remain expensive, oversized and complex, but a new generation of smaller, more affordable sensors should open up new applications. Last year researchers at the Massachusetts Institute of Technology used conventional fabrication methods to put a diamond-based quantum sensor on a silicon chip, squeezing multiple, traditionally bulky components onto a square a few tenths of a millimeter wide. The prototype is a step toward low-cost, mass-produced quantum sensors that work at room temperature and that could be used for any application that involves taking fine measurements of weak magnetic fields.

Quantum systems remain extremely susceptible to disturbances, which could limit their application to controlled environments. But governments and private investors are throwing money at this and other challenges, including those of cost, scale and complexity; the U.K., for example, has put £315 million into the second phase of its National Quantum Computing Program (2019–2024). Industry analysts expect quantum sensors to reach the market in the next three to five years, with an initial emphasis on medical and defense applications.



ENERGY Green Hydrogen

Zero-carbon energy to supplement wind and solar

By Jeff Carbeck

WHEN HYDROGEN BURNS, the only by-product is water which is why hydrogen has been an alluring zerocarbon energy source for decades. Yet the traditional process for producing hydrogen, in which fossil fuels are exposed to steam, is not even remotely zerocarbon. Hydrogen produced this way is called gray hydrogen; if the CO_2 is captured and sequestered, it is called blue hydrogen.

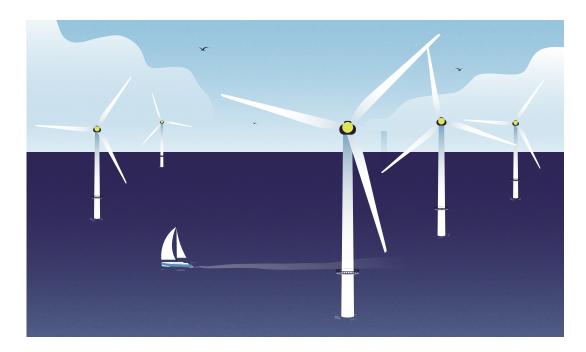
Green hydrogen is different. It is produced through electrolysis, in which machines split water into hydrogen and oxygen, with no other by-products. Historically, electrolysis required so much electricity that it made little sense to produce hydrogen that way. The situation is changing for two reasons. First, significant amounts of excess renewable electricity have become available at grid scale; rather than storing excess electricity in arrays of batteries, the extra electricity can be used to drive the electrolysis of water, "storing" the electricity in the form of hydrogen. Second, electrolyzers are getting more efficient.

Companies are working to develop electrolyzers that can produce green hydrogen as cheaply as gray or blue hydrogen, and analysts expect them to reach that goal in the next decade. Meanwhile energy companies are starting to integrate electrolyzers directly into renewable power projects. For example, a consortium of companies behind a project called Gigastack plan to equip Ørsted's Hornsea Two offshore wind farm with 100 megawatts of electrolyzers to generate green hydrogen at an industrial scale.

Current renewable technologies such as solar and wind can decarbonize the energy sector by as much as 85 percent by replacing gas and coal with clean electricity. Other parts of the economy, such as shipping and manufacturing, are harder to electrify because they often require fuel that is high in energy density or heat at high temperatures. Green hydrogen has potential in these sectors. The Energy Transitions Commission, an industry group, says green hydrogen is one of four technologies necessary for meeting the Paris Agreement goal of abating more than 10 gigatons of carbon dioxide a year from the most challenging industrial sectors, among them mining, construction and chemicals.

Although green hydrogen is still in its infancy, countries—especially those with cheap renewable energy—are investing in the technology. Australia wants to export hydrogen that it would produce using its plentiful solar and wind power. Chile has plans for hydrogen in the country's arid north, where solar electricity is abundant. China aims to put one million hydrogen fuel–cell vehicles on the road by 2030.

Similar projects are underway in South Korea, Malaysia, Norway and the U.S., where the state of California is working to phase out fossil-fuel buses by 2040. And the European Commission's recently published 2030 hydrogen strategy calls for increasing hydrogen capacity from 0.1 gigawatt today to 500 gigawatts by 2050. All of which is why, earlier this year, Goldman Sachs predicted that green hydrogen will become a \$12-trillion market by 2050.



TOP 10 EMERGING TECHNOLOGIES OF 2020





SYNTHETIC BIOLOGY Whole-Genome Synthesis

Next-level cell engineering

By Andrew Hessel and Sang Yup Lee

EARLY IN THE COVID-19 PANDEMIC, scientists in China uploaded the virus's genetic sequence (the blueprint for its production) to genetic databases. A Swiss group then synthesized the entire genome and produced the virus from it—essentially teleporting the virus into their laboratory for study without having to wait for physical samples. Such speed is one example of how whole-genome printing is advancing medicine and other endeavors.

Whole-genome synthesis is an extension of the booming field of synthetic biology. Researchers use software to design genetic sequences that they produce and introduce into a microbe, thereby reprogramming the microbe to do desired work—such as making a new medicine. So far genomes mainly get light edits. But improvements in synthesis technology and software are making it possible to print ever larger swaths of genetic material and to alter genomes more extensively.

Viral genomes, which are tiny, were produced first, starting in 2002 with the poliovirus's roughly 7,500 nucleotides, or code letters. As with the coronavirus, these synthesized viral genomes have helped investigators gain insight into how the associated viruses spread and cause disease. Some are being designed to serve in the production of vaccines and immunotherapies.

Writing genomes that contain millions of nucleotides, as in bacteria and yeast, has become tractable as well. In 2019 a team printed a version of the Escherichia coli genome that made room for codes that could force the bacterium to do scientists' bidding. Another team has produced an initial version of the brewer's yeast genome, which consists of almost 11 million code letters. Genome design and synthesis at this scale will allow microbes to serve as factories for producing not only drugs but any number of substances. They could be engineered to sustainably produce chemicals, fuels and novel construction materials from nonfood biomass or even waste gases such as carbon dioxide.

Many scientists want the ability to write larger genomes, such as those from plants, animals and humans. Getting there requires greater investment in design software (most likely incorporating artificial intelligence) and in faster, cheaper methods for synthesizing and assembling DNA sequences at least millions of nucleotides long. With sufficient

funding, the writing of genomes on the billion-nucleotide scale could be a reality before the end of this decade. Investigators have many applications in mind, including the design of plants that resist pathogens and an ultrasafe human cell line—impervious, say, to virus infections, cancer and radiation—that could be the basis for cellbased therapies or for biomanufacturing. The ability to write our own genome will inevitably emerge, enabling doctors to cure many, if not all, genetic diseases.

Of course, whole-genome engineering could be misused, with the chief fear being weaponized pathogens or their toxin-generating components. Scientists and engineers will need to devise a comprehensive biological security filter: a set of existing and novel technologies able to detect and monitor the spread of new threats in real time. Investigators will need to invent testing strategies that can scale rapidly. Critically, governments around the world must cooperate much more than they do now.

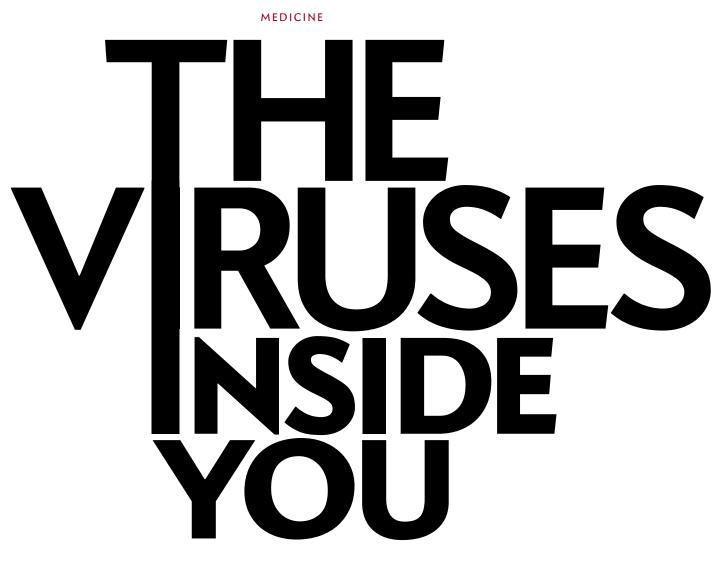
The Genome Project-write, a consortium formed in 2016, is positioned to facilitate this safety net. The project includes hundreds of scientists, engineers and ethicists from more than a dozen countries who develop technologies, share best practices, carry out pilot projects, and explore ethical, legal and societal implications.

FROM OUR ARCHIVES

Top 10 Emerging Technologies of 2019. World Economic Forum and Scientific American; December 2019.

scientificamerican.com/magazine/sa





Trillions of viruses make up the human virome. Some can harm us, but some could help us, if we can figure out how to use them

By David Pride

Illustration by Harry Campbell

David Pride is an infectious disease specialist and associate professor of pathology at the University of California, San Diego. His laboratory focuses on the role that microbial communities play in human homeostasis, health and disease.





HIS YEAR MILLIONS OF PEOPLE AROUND THE WORLD HAVE RADICALLY changed their way of life to avoid contact with other people and, thus, <u>the novel coronavirus</u>. Despite social distancing, many have still gotten sick in part from other viral infections. That is because, as scientists are increasingly learning, many viruses are lurking quietly in the human body, hidden away in cells in the lungs, blood and nerves and inside the multitudes of microbes that colonize our gut.

Biologists estimate that 380 trillion viruses are living on and inside your body right now-10 times the number of bacteria. Some can cause illness, but many simply coexist with you. In late 2019, for example, researchers at the University of Pennsylvania discovered 19 different strains of redondovirus in the respiratory tract; a handful were associated with periodontal disease or lung disease, but others could possibly fight respiratory illnesses. Scientists' rapidly expanding knowledge makes it clear that we are not made up primarily of "human" cells that are occasionally invaded by microbes; our body is really a superorganism of cohabitating cells, bacteria, fungi and most numerous of all: viruses. The latest counts indicate that as much as half of all the biological matter in your body is not human.

A decade ago researchers were barely aware that the human virome existed. Today we see the vast virome as an integral part of the larger human microbiome, a crazy quilt of passive and active microscopic organisms that occupy almost every corner of our being. We have been mapping the virome for 10 years, and the deeper we investigate, the more the virome looks like a partnership that can influence our daily lives positively as well as negatively. Recent research shows we could even harness the virome to promote our own health. Investigators at the Rockefeller University, for example, have purified an enzyme from a virus that kills bacteria found in patients who are struggling against methicillin-resistant staphylococcal infection. The results are so encouraging that the Food and Drug Administration has designated the enzyme as a "breakthrough therapy," and it is now in phase 3 clinical trials. Today we routinely speak about the "good" and "bad" bacteria in our lives. Viruses fall into the same categories. The challenge now is to figure out how to stop the bad ones and promote the good ones.

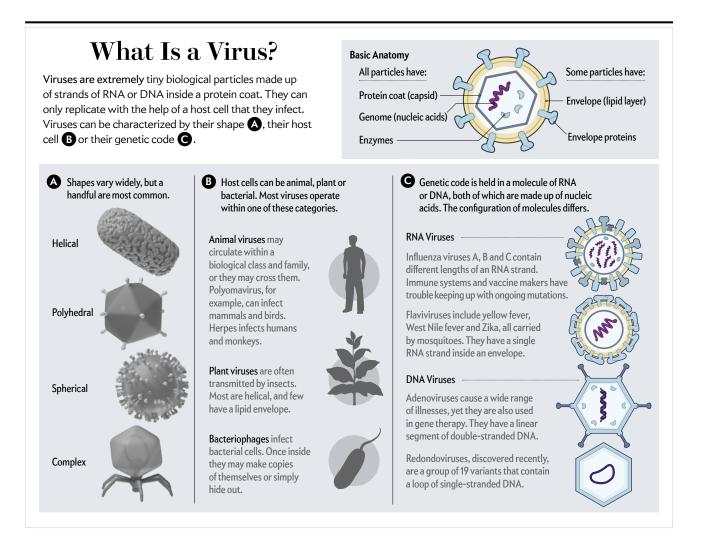
INFECTED AT BIRTH

THE HUMAN BODY is a rich environment for microbes, replete with proteins, fats and carbohydrates. Many viruses have figured out how to peacefully thrive in it without making us sick.

Viruses need to invade host cells to reproduce, and they are adept at exploiting all the options in our body. A dozen years ago inexpensive genome sequencing led us to discover plentiful viruses in the mouth and gut. By 2013 or so scientists located viruses on the skin and in the respiratory tract, blood and urine. Most recently, we have found them in even more surprising places. In September 2019, for example, Chandrabali Ghose and our colleagues and I published details about viruses that we discovered in the cerebrospinal fluid of adults who were undergoing testing for various conditions. The viruses belonged to several different families and were not associated with any known disease. We also found the same viruses in blood plasma, joint fluid and breast milk. Scientists knew that a few rare, infectious viruses, notably herpes, could sneak into cerebrospinal fluid, but finding random viruses that seemed to be mere bystanders was a surprise. The central nervous system, which is supposed to be a sterile environment, is colonized by a somewhat diverse viral community.

It appears that our viromes begin to accumulate when we are born. Studies reveal a high diversity of viruses in the infant gut shortly after birth, suggesting that they probably come from the babies' mothers, some ingested from breast milk. Some of these viruses decline in number as infants grow to weeks or months old; others enter their bodies from the air, water, food and other people. These viruses grow in number and diversity, infecting cells where they will persist for years. Infant viromes are unstable, whereas adult viromes are relatively stable. Anelloviruses, a family of 200 different species, are present in almost everyone as we get older. This mirrors what we observe for bacteria as well.

Many of the viruses living inside us do not target our cells. Instead they look for the bacteria in our microbiomes. Known as <u>bacteriophages</u>, or phages, these viruses sneak inside bacterial cells, use the machinery there to make copies of themselves, then often burst out to infect more bacteria, killing their host cells in the process. Bacteriophages are nearly



ubiquitous in nature. If you look hard enough, you will find them in soil, in any source of water from the ocean to your tap at home, and in extreme environments such as acid mines, the Arctic and hot springs. You will even find them floating in the air. They persist in all these places because they are hunting the bacteria that live in all these places. We humans are just another hunting ground.

In 2017 Sophie Nguyen and Jeremy Barr, then at San Diego State University, demonstrated that many phages get to their final locations in the body by crossing through mucosal membranes. In laboratory experiments, phages worked through membranes that line the intestine, lung, liver, kidney, even the brain. But when they randomly cross into a place such as the central nervous system, where there are few bacteria to be hosts, they may have no way to replicate and may ultimately perish.

YOUR PERSONAL VIRUS PROFILE

THE VIROME CAN VARY greatly from one part of the body to another. When Ghose and I looked for viruses in unexpected places, we also determined that viruses in the mouth are different from viruses in the gut, which are different from viruses in urine or in blood. We knew this was the case for bacteria, but early on we did not have enough data for viruses. Although it is not hard to find volunteers who will spit in a cup, it is hard to get them to provide stool or blood samples and to persuade universities to sign off on obtaining and processing these samples. When we do have the goods, we must filter out the bacteria, leaving tiny bits of viral material we can examine under a microscope and insert into a machine that sequences the nucleic acids that encode the genes that are present. Still, researchers have done enough of this work now to be able to tell what part of the body they are examining just by noting the viruses present.

My colleague Melissa Ly of the University of California, San Diego, and I have also shown that by comparing the viromes of unrelated people we can determine if any of them live together. Although different people can have significantly different viromes, people who cohabitate appear to share about 25 percent of the viruses in their viromes. Viruses can be transmitted from one household member to the other not just through typical contagious means such as coughing but also through casual contact and sharing sinks, toilets, desks and food. Although we have only studied small numbers of people, the data show that nonromantic roommates share a similar percentage of viruses as romantic roommates do. Intimate contact seems to make little difference; just living in the same space is enough.

The puzzle is tricky, however. Shira Abeles, also at U.C. San Diego, has identified big differences in the oral viromes of men and women; hormones could be

The Human Virome

Our bodies are full of viruses that come and go or that persist for years. Some virus families, such as herpes, cause multiple diseases. Others, less well understood, may be benign, even those found in almost all people worldwide, such as crAssphage.

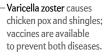
Herpes: The Chameleon

There are more than 100 herpesviruses, each slightly different. Nine infect humans, notably the following:

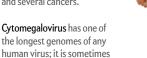


 Herpes simplex type 1 creates most cold sores.
Like other herpesviruses, it can lie dormant in nerve cells.

Herpes simplex type 2 _____ produces most genital herpes transmitted by physical contact between people.



Epstein-Barr can cause mononucleosis and is also associated with lupus and several cancers.

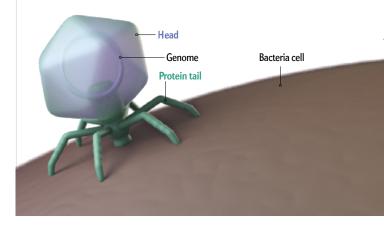


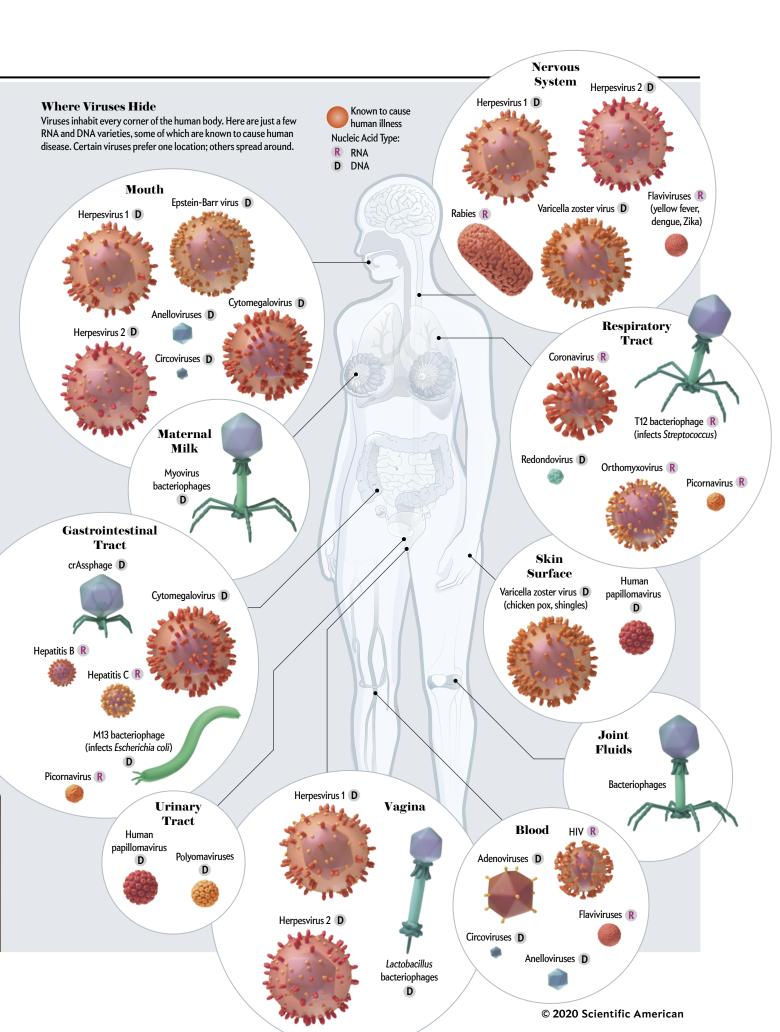


implicated in pneumonia.

Common but Mysterious: crAssphage

Phage viruses infect bacteria. The crAssphage is found in humans worldwide, as well as in termites, plant roots, groundwater and ocean sediment. Researchers are not sure how it affects people; so far there is no evidence linking it to disease. It is named after the computer program that discovered it from data about human feces.





the reason, but no one has demonstrated such a connection. We do know that viromes can vary considerably with geographic populations. For example, there is less diversity in the viromes of individuals in Western countries than there is among individuals in non-Western countries. These differences may be related to both diet and environment.

VAGABONDS OR FREELOADERS?

MANY VIRUSES in our virome infect bacteria, but a smaller proportion infect cells in our tissues directly. These viruses may be in the minority because our immune system suppresses them. Iwijn De Vlaminck, then at Stanford University, demonstrated that when a person's immune system is strongly challenged—for example, when someone has received an organ transplant and must take immunosuppressing drugs to avoid rejecting the organ the presence of certain viruses increases dramatically. In these cases, we see a rise in both viruses

People who cohabitate share about 25 percent of the viruses in their viromes, just by virtue of living in the same space.

known to cause disease and those that do not. This observation suggests that under normal circumstances our immune system keeps the virome in check, but when immunity is hampered, viruses can multiply readily.

We may be seeing this kind of opportunism with COVID-19. People who get sick from the <u>SARS-CoV-2 virus</u>, particularly those with severe illness, may develop coinfections. The most common are a secondary bacterial pneumonia, or bacteremia (a rise of bacteria in the bloodstream), involving organisms such as *Staphylococcus aureus* and *Streptococcus pneumoniae*. Though less common, we have also seen viral coinfections such as influenza, respiratory syncytial virus and adenovirus. Viruses lurking in the virome may also reactivate, such as Epstein-Barr virus and cytomegalovirus. When the immune system is paying attention to COVID-19, the patient may be more susceptible to other viral outbreaks.

Many phages, despite being hunters, live in harmony with their prey for a long time and may never break out. A virus is just a ball of protein enveloping a molecule of genetic instructions—the virus's genetic code. When some phages infect a bacterium, they integrate their genome into the bacterium's genome. Although certain viruses reproduce immediately, killing their host bacteria, other phages just persist inside their host, as if in quiet hibernation. This is probably a survival strategy; when the host bacterium divides, creating a copy of its genome, it copies the phage genome as well. In this model, the survival of the host determines the survival of the phage, so the phage has a vested interest in maintaining its host. It is clear why such a strategy benefits the phage but not so clear how it could benefit the bacteria. For whatever reason, it seems that many bacteria in the body have grown accustomed to living with their phages.

When the opportunity arises, hibernating phages may awaken and produce many progeny, killing their host cells. Sometimes the exiting phages take bacterial genes along with them. This payload can at times benefit the next bacteria the phages infect. I have found phages in saliva, for example, carrying genes that help bacteria evade our immune system. Some phages even carry

> genes that help bacteria resist antibiotics. Phages have no need for such genes, because phages cannot be killed by antibiotics, so when they provide the genes to bacteria they promote the hosts' survival—synonymous with survival of the phages. We see these kinds of transfers often.

> Phages can take protection of their host further. The bacterium *Pseudomonas aeruginosa*, best

known for causing pneumonia, triggers a number of illnesses. People who have lung diseases such as cystic fibrosis find it nearly impossible to clear this bacterium from their lungs, even when taking antibiotics designed to kill it. Some *P. aeruginosa* have integrated what are called filamentous phages into their genomes. In 2019 researchers led by a group at Stanford, including Elizabeth Burgener and Paul Bollyky, discovered that filamentous phages can form a protective cloak—layers of carbohydrates and proteins that help bacteria hide from antibiotics. This allows the bacteria to shelter in place until the antibiotics go away, living to cause infection another day.

VIRUSES THAT HELP US

IT IS NOT A BIG LEAP to wonder whether we can harness the viruses living within us to improve our health. We have already found a few cases in which this happens naturally. As phages move around the body looking for bacteria, some of them bind to cells on the surface of mucosal membranes, such as those that line the nose, throat, stomach and intestines. The phages cannot replicate there, but they can lie in wait for a vulnerable host to come by.

This process could theoretically protect us from some illnesses. Say you eat food contaminated with Salmonella bacteria. If the bacteria brush along the stomach's membrane, phages there could ostensibly infect the bacteria and kill them before they can cause disease. In this way, phages may serve as a de facto immune system that protects us against disease. No one has proved this yet, but in 2019 a research group in Finland showed that phages bound to mucus in pigs and rainbow trout persisted there for seven days and protected against one kind of bacterium that infects these animals.

One phage getting a lot of attention is crAssphage, discovered in 2014 by Bas Dutilh of the Radboud Institute in the Netherlands. Studies since then have shown that it inhabits most people around the world—except, it seems, for traditional hunter-gatherer populations. It is unusual to find the exact same virus spread so far and wide, and no one has linked it to any disease. Scientists think it controls the prevalence of a common gut bacterium called *Bacteroides*. If so, we might be able to exploit it to improve gastrointestinal conditions. It is so prevalent in human feces that researchers now test for it in drinking water to see if the water has been contaminated by sewage.

Physicians are especially interested in phages that might counteract the aggressive rise of antibiotic-resistant bacteria. Development of new antibiotics has failed to keep pace. The World Health Organization estimates that by 2050 these pathogens will cause at least 10 million deaths annually, so alternative therapies are vital. Phages were discovered more than 100 years ago, and physicians tried to use them to treat bacteria that cause disease, though without great success. In the 1940s antibiotics replaced phages in most of the world because the drugs were much more effective and much easier to use. Now some medical researchers, such as the Rockefeller University investigators who used a phage enzyme to fight methicillinresistant Staphylococcus infection, are taking a new look at phages.

For years most physicians have been afraid to administer phages because they did not know whether the human immune system would overreact, causing dangerous levels of inflammation. Phages for therapeutic use are grown in bacteria, and if the bacteria are not completely removed before the phages are administered, the bacteria can trigger an overly aggressive immune response. Today we have more sophisticated methods of purifying phages, and worries about adverse reactions have largely subsided.

What really limits the use of phages to treat infectious disease is that effective viruses are hard to find. For many years researchers have combed through natural habitats for phages that might be active against bacteria that cause human disease. Now that we know that viruses are plentiful in feces, saliva and sputum, researchers have realized that one of the richest sources of phages may be local sewage-processing plants.

A few such phages are already being used for experimental treatments. In a landmark 2016 case overseen by Robert Schooley, also at U.C. San Diego, doctors used phages from sewage, as well as those from environmental sources, to successfully treat Tom Patterson, a professor at the school who was in multiorgan failure because of *Acinetobacter baumannii*, a notoriously drug-resistant bacteria.

IMPROVED HEALTH

AS WE LEARN MORE about the roles of viruses in the human virome, we may uncover more therapeutic possibilities. Alejandro Reyes of Washington University in St. Louis has shown that phages in mice can shape the rodents' bacterial communities, although we are not sure what changes first: the viruses or the bacteria. If the viral communities change first, they can sculpt the bacterial communities to serve them. If the bacterial communities change first, the viral communities are likely just adapting so they can infiltrate the reshaped bacteria. Researchers have shown that viromes can change significantly in periodontal disease and in inflammatory bowel diseases.

Although it will take a long time for us to unravel the human virome, it is important to consider how far we have come in just 10 years. A decade ago many scientists thought of the microbiome as a kind of passive layer of tiny organisms inside the body, mostly in the gut. Now we know that although some parts of the microbiome are indeed stable, some parts are active and changing. And it is beginning to look like the most dynamic players are the viruses. A 2018 study of brain tissue donated by people who had died of Alzheimer's disease revealed high levels of herpesviruses. Then, in May 2020, investigators at Tufts University and the Massachusetts Institute of Technology, who have developed brainlike tissue in the lab, infected their tissue with herpes simplex 1, and the tissue became full of amyloid plaquelike formations akin to those that riddle the brains of people who have Alzheimer's. It is startling to realize that we could discover remarkable roles for old viruses.

As we look deeper, we may find new categories of viruses that impact human health, as well as new ways to exploit viruses to manipulate our microbiome and protect us from disease. If we humans can figure out how to manage the bad viruses and exploit the good ones, we could help ourselves become stronger superorganisms.

FROM OUR ARCHIVES

Is Phage Therapy Here to Stay? Charles Schmidt; November 2019.

scientificamerican.com/magazine/sa

THE ATTENTION ECONOMY Understanding how algorithms and manipulators exploit our cognitive

SOCIAL MEDIA

vulnerabilities empowers us to fight back

By Filippo Menczer and Thomas Hills

Illustration by Cristina Spanò

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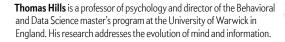
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Filippo Menczer is Distinguished Professor of Informatics and Computer Science and director of the Observatory on Social Media at Indiana University Bloomington. He studies the spread of disinformation and develops tools for countering social media manipulation.





ONSIDER ANDY, WHO IS WORRIED ABOUT CONTRACTING COVID-19. UNABLE TO READ all the articles he sees on it, he relies on trusted friends for tips. When one opines on Facebook that pandemic fears are overblown, Andy dismisses the idea at first. But then the hotel where he works closes its doors, and with his job at risk, Andy starts wondering how serious the threat from the new virus really is. No one he knows has died, after all. A colleague posts an article about the COVID "scare" having been created by

Big Pharma in collusion with corrupt politicians, which jibes with Andy's distrust of government. His Web search quickly takes him to articles claiming that COVID-19 is no worse than the flu. Andy joins an online group of people who have been or fear being laid off and soon finds himself asking, like many of them, "What pandemic?" When he learns that several of his new friends are planning to attend a rally demanding an end to lockdowns, he decides to join them. Almost no one at the massive protest, including him, wears a mask. When his sister asks about the rally, Andy shares the conviction that has now become part of his identity: COVID is a hoax.

> This example illustrates a minefield of cognitive biases. We prefer information from people we trust, our in-group. We pay attention to and are more likely to share information about risks—for Andy, the risk of losing his job. We search for and remember things that fit well with what we already know and understand. These biases are products of our evolutionary past, and for tens of thousands of years, they served us well. People who behaved in accordance with them—for example, by staying away from the overgrown pond bank where someone said there was a viper—were more likely to survive than those who did not.

> Modern technologies are amplifying these biases in harmful ways, however. Search engines direct Andy to sites that inflame his suspicions, and social media connects him with like-minded people, feeding his fears. Making matters worse, bots—automated social media accounts that impersonate humans—enable

misguided or malevolent actors to take advantage of his vulnerabilities.

Compounding the problem is the proliferation of online information. Viewing and producing blogs, videos, tweets and other units of information called memes has become so cheap and easy that the information marketplace is inundated. Unable to process all this material, we let our cognitive biases decide what we should pay attention to. These mental shortcuts influence which information we search for, comprehend, remember and repeat to a harmful extent.

The need to understand these cognitive vulnerabilities and how algorithms use or manipulate them has become urgent. At the University of Warwick in England and at Indiana University Bloomington's Observatory on Social Media (OSoMe, pronounced "awesome"), our teams are using cognitive experiments, simulations, data mining and artificial intelligence to comprehend the cognitive vulnerabilities of social media users. Insights from psychological studies on the evolution of information conducted at Warwick inform the computer models developed at Indiana, and vice versa. We are also developing analytical and machine-learning aids to fight social media manipulation. Some of these tools are already being used by journalists, civil-society organizations and individuals to detect inauthentic actors, map the spread of false narratives and foster news literacy.

INFORMATION OVERLOAD

THE GLUT OF INFORMATION has generated intense competition for people's attention. As Nobel Prize-winning economist and psychologist Herbert A. Simon noted, "What information consumes is rather obvious: it consumes the attention of its recipients." One of the first consequences of the so-called attention economy is the loss of high-quality information. The OSoMe team demonstrated this result with a set of simple simulations. It represented users of social media such as Andy, called agents, as nodes in a network of online acquaintances. At each time step in the simulation, an agent may either create a meme or reshare one that he or she sees in a news feed. To mimic limited attention, agents are allowed to view only a certain number of items near the top of their news feeds.

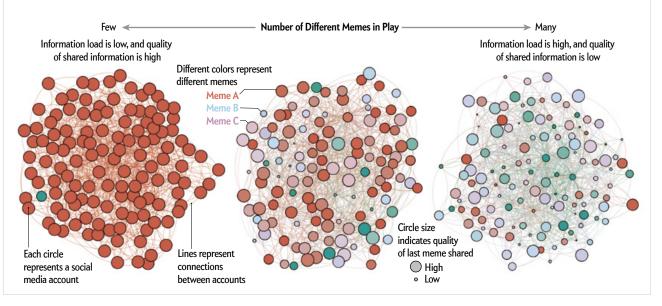
Running this simulation over many time steps, Lilian Weng of OSoMe <u>found</u> that as agents' attention became increasingly limited, the propagation of memes came to reflect the power-law distribution of actual social media: the probability that a meme would be shared a given number of times was roughly an inverse power of that number. For example, the likelihood of a meme being shared three times was approximately nine times less than that of its being shared once.

This winner-take-all popularity pattern of memes, in which most are barely noticed while a few spread widely, could not be explained by some of them being more catchy or somehow more valuable: the memes in this simulated world had no intrinsic quality. Virality resulted purely from the statistical consequences of information proliferation in a social network of agents with limited attention. Even when agents preferentially shared memes of higher quality, researcher Xiaoyan Qiu, then at OSoMe, observed little improvement in the overall quality of those shared the most. Our models revealed that even when we want to see and share high-quality information, our inability to view everything in our news feeds inevitably leads us to share things that are partly or completely untrue.

Cognitive biases greatly worsen the problem. In a set of groundbreaking studies in 1932, psychologist Frederic Bartlett told volunteers a Native American legend about a young man who hears war cries and, pursuing them, enters a dreamlike battle that eventually leads to his real death. Bartlett asked the vol-

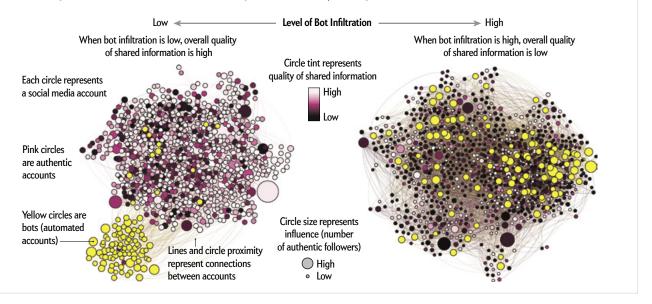
Information Overload

Our social media newsfeeds are often so full that many of us can view only the top few items, from which we choose to reshare or retweet. Researchers at the Observatory on Social Media (OSoMe) at Indiana University Bloomington simulated this limited capacity to pay attention. Each node in the model network represents a user, linked by lines to friends or followers who receive the items they share or reshare. Investigators found that as the number of memes in the network rises (*toward the right*), the quality of those that propagate widely falls (*circles become smaller*). So information overload can alone explain why fake news can become viral.



Pollution by Bots

Bots, or automated accounts that impersonate human users, greatly reduce the quality of information in a social network. In one computer simulation, OSoMe researchers included bots (modeled as agents that tweet only memes of zero quality and retweet only one another) in the social network. They found that when less than 1 percent of human users follow bots, information quality is high (*left*). But when the percentage of bot infiltration exceeds 1, poor-quality information propagates throughout the network (*right*). In real social networks, just a few early upvotes by bots can make a fake news item become viral.



unteers, who were non-Native, to recall the rather confusing story at increasing intervals, from minutes to years later. He found that as time passed, the rememberers tended to distort the tale's culturally unfamiliar parts such that they were either lost to memory or transformed into more familiar things. We now know that our minds do this all the time: they adjust our understanding of new information so that it fits in with what we already know. One consequence of this so-called confirmation bias is that people often seek out, recall and understand information that best confirms what they already believe.

This tendency is extremely difficult to correct. Experiments consistently show that even when people encounter balanced information containing views from differing perspectives, they tend to find supporting evidence for what they already believe. And when people with divergent beliefs about emotionally charged issues such as climate change are shown the same information on these topics, they become even more committed to their original positions.

Making matters worse, search engines and social media platforms provide personalized recommendations based on the vast amounts of data they have about users' past preferences. They prioritize information in our feeds that we are most likely to agree with—no matter how fringe—and shield us from information that might change our minds. This makes us easy targets for polarization. Nir Grinberg and his co-workers at Northeastern University recently showed that conservatives in the U.S. are more receptive to misinformation. But our own analysis of consumption of low-quality information on Twitter shows that the vulnerability applies to both sides of the political spectrum, and no one can fully avoid it. Even our ability to detect online manipulation is affected by our political bias, though <u>not symmetrically</u>: Republican users are more likely to mistake bots promoting conservative ideas for humans, whereas Democrats are more likely to mistake conservative human users for bots.

SOCIAL HERDING

IN NEW YORK CITY IN AUGUST 2019, people began running away from what sounded like gunshots. Others followed, some shouting, "Shooter!" Only later did they learn that the blasts came from a backfiring motorcycle. In such a situation, it may pay to run first and ask questions later. In the absence of clear signals, our brains use information about the crowd to infer appropriate actions, similar to the behavior of schooling fish and flocking birds.

Such social conformity is pervasive. In a fascinating 2006 study involving 14,000 Web-based volunteers, Matthew Salganik, then at Columbia University, and his colleagues found that when people can see what music others are downloading, they end up downloading similar songs. Moreover, when people were isolated into "social" groups, in which they could see the preferences of others in their circle but had no information about outsiders, the choices of individual groups rapidly diverged. But the preferences of "nonsocial" groups, where no one knew about others' choices, stayed relatively stable. In other words, social groups create a pressure toward conformity so powerful that it can overcome individual preferences, and by amplifying random early differences, it can cause segregated groups to diverge to extremes.

Social media follows a similar dynamic. We confuse popularity with quality and end up copying the behavior we observe. Experiments on Twitter by Bjarke Mønsted and his colleagues at the Technical University of Denmark and the University of Southern California indicate that information is transmitted via "complex contagion": when we are repeatedly exposed to an idea, typically from many sources, we are more likely to adopt and reshare it. This social bias is further amplified by what psychologists call the "mere exposure" effect: when people are repeatedly exposed to the same stimuli, such as certain faces, they grow to like those stimuli more than those they have encountered less often.

Such biases translate into an irresistible urge to pay attention to information that is going viral—if everybody else is talking about it, it must be important. In addition to showing us items that conform with our views, social media platforms such as Facebook, Twitter, YouTube and Instagram place pop-

ular content at the top of our screens and show us how many people have liked and shared something. Few of us realize that these cues do not provide independent assessments of quality.

In fact, programmers who design the algorithms for ranking memes on social media assume that the "wisdom of crowds" will quickly identify high-quality items; they use popularity as a proxy for quality. Our analysis of vast amounts of anonymous data about clicks shows that all platforms—social media, search engines and news sites—preferentially serve up information from a narrow subset of popular sources.

To understand why, we modeled how they combine signals for quality and popularity in their rankings. In this model, agents with limited attention—those who see only a given number of items at the top of their news feeds—are also more likely to click on memes ranked higher by the platform. Each item has intrinsic quality, as well as a level of popularity determined by how many times it has been clicked on. Another variable tracks the extent to which the ranking relies on popularity rather than quality. <u>Simulations of this</u> <u>model reveal</u> that such algorithmic bias typically suppresses the quality of memes even in the absence of human bias. Even when we want to share the best information, the algorithms end up misleading us.

ECHO CHAMBERS

MOST OF US DO NOT BELIEVE we follow the herd. But our confirmation bias leads us to follow others who are like us, a dynamic that is sometimes referred to as homophily—a tendency for like-minded people to connect with one another. Social media amplifies homophily by allowing users to alter their social network structures through following, unfriending, and so on. The result is that people become segregated into large, dense and increasingly misinformed communities commonly described as echo chambers.

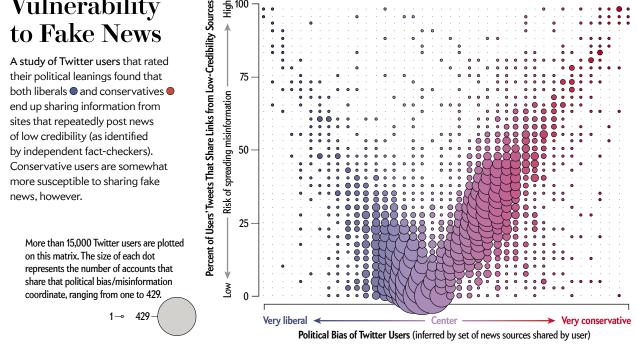
At OSoMe, we explored the emergence of online echo chambers through another simulation, <u>Echo-Demo</u>. In this model, each agent has a political opinion represented by a number ranging from –1 (say, liberal) to +1 (conservative). These inclinations are reflected in agents' posts. Agents are also influenced by the opinions they see in their news feeds, and they can unfollow users with dissimilar opinions. Starting with random initial networks and opinions, we found that the combination of social influence and unfollowing greatly accelerates the formation of polarized and segregated communities.

Information that passes from person to person along a chain becomes more negative and more resistant to correction.

Indeed, the political echo chambers on Twitter are so extreme that individual users' political leanings can be predicted with high accuracy: you have the same opinions as the majority of your connections. This chambered structure efficiently spreads information within a community while insulating that community from other groups. In 2014 our research group was targeted by a disinformation campaign claiming that we were part of a politically motivated effort to suppress free speech. This false charge spread virally mostly in the conservative echo chamber, whereas debunking articles by fact-checkers were found mainly in the liberal community. Sadly, such segregation of fake news items from their fact-check reports is the norm.

Social media can also increase our negativity. In a recent laboratory study, Robert Jagiello, also at Warwick, <u>found</u> that socially shared information not only bolsters our biases but also becomes more resilient to correction. He investigated how information is passed from person to person in a so-called social diffusion chain. In the experiment, the first person in the chain read a set of articles about either nuclear power or food additives. The articles were designed to be balanced, containing as much positive information (for example, about less carbon pollution or lon-

Vulnerability



ger-lasting food) as negative information (such as risk of meltdown or possible harm to health).

The first person in the social diffusion chain told the next person about the articles, the second told the third, and so on. We observed an overall increase in the amount of negative information as it passed along the chain-known as the social amplification of risk. Moreover, work by Danielle J. Navarro and her colleagues at the University of New South Wales in Australia found that information in social diffusion chains is most susceptible to distortion by individuals with the most extreme biases.

Even worse, social diffusion also makes negative information more "sticky." When Jagiello subsequently exposed people in the social diffusion chains to the original, balanced information-that is, the news that the first person in the chain had seen-the balanced information did little to reduce individuals' negative attitudes. The information that had passed through people not only had become more negative but also was more resistant to updating.

A 2015 study by OSoMe researchers Emilio Ferrara and Zeyao Yang analyzed empirical data about such "emotional contagion" on Twitter and found that people overexposed to negative content tend to then share negative posts, whereas those overexposed to positive content tend to share more positive posts. Because negative content spreads faster than positive content, it is easy to manipulate emotions by creating narratives that trigger negative responses such as fear and anxiety. Ferrara, now at the University of Southern California, and his colleagues at the Bruno

Kessler Foundation in Italy have shown that during Spain's 2017 referendum on Catalan independence, social bots were leveraged to retweet violent and inflammatory narratives, increasing their exposure and exacerbating social conflict.

RISE OF THE BOTS

INFORMATION QUALITY is further impaired by social bots, which can exploit all our cognitive loopholes. Bots are easy to create. Social media platforms provide so-called application programming interfaces that make it fairly trivial for a single actor to set up and control thousands of bots. But amplifying a message, even with just a few early upvotes by bots on social media platforms such as Reddit, can have a huge impact on the subsequent popularity of a post.

At OSoMe, we have developed machine-learning algorithms to detect social bots. One of these, Botometer, is a public tool that extracts 1,200 features from a given Twitter account to characterize its profile, friends, social network structure, temporal activity patterns, language and other features. The program compares these characteristics with those of tens of thousands of previously identified bots to give the Twitter account a score for its likely use of automation.

In 2017 we estimated that up to 15 percent of active Twitter accounts were bots-and that they had played a key role in the spread of misinformation during the 2016 U.S. election period. Within seconds of a fake news article being posted-such as one claiming the Clinton campaign was involved in occult rituals-it would be tweeted by many bots, and humans, beguiled by the

apparent popularity of the content, would retweet it.

Bots also influence us by pretending to represent people from our in-group. A bot only has to follow, like and retweet someone in an online community to quickly infiltrate it. OSoMe researcher Xiaodan Lou developed another model in which some of the agents are bots that infiltrate a social network and share deceptively engaging low-quality content-think of clickbait. One parameter in the model describes the probability that an authentic agent will follow botswhich, for the purposes of this model, we define as agents that generate memes of zero quality and retweet only one another. Our simulations show that these bots can effectively suppress the entire ecosystem's information quality by infiltrating only a small fraction of the network. Bots can also accelerate the formation of echo chambers by suggesting other inauthentic accounts to be followed, a technique known as creating "follow trains."

Some manipulators play both sides of a divide through separate fake news sites and bots, driving political polarization or monetization by ads. At OSoMe, we recently <u>uncovered a network of inauthen-</u> <u>tic accounts</u> on Twitter that were all coordinated by the same entity. Some pretended to be pro-Trump supporters of the Make America Great Again campaign, whereas others posed as Trump "resisters"; all asked for political donations. Such operations amplify content that preys on confirmation biases and accelerate the formation of polarized echo chambers.

CURBING ONLINE MANIPULATION

UNDERSTANDING OUR COGNITIVE BIASES and how algorithms and bots exploit them allows us to better guard against manipulation. OSoMe has produced a number of tools to help people understand their own vulnerabilities, as well as the weaknesses of social media platforms. One is a mobile app called <u>Fakey</u> that helps users learn how to spot misinformation. The game simulates a social media news feed, showing actual articles from low- and high-credibility sources. Users must decide what they can or should not share and what to fact-check. Analysis of data from Fakey confirms the prevalence of online social herding: users are more likely to share low-credibility articles when they believe that many other people have shared them.

Another program available to the public, called Hoaxy, shows how any extant meme spreads through Twitter. In this visualization, nodes represent actual Twitter accounts, and links depict how retweets, quotes, mentions and replies propagate the meme from account to account. Each node has a color representing its score from Botometer, which allows users to see the scale at which bots amplify misinformation. These tools have been used by investigative journalists to uncover the roots of misinformation campaigns, such as one pushing the "pizzagate" conspiracy in the U.S. They also helped to detect bot-driven voter-suppression efforts during the 2018 U.S. midterm election. Manipulation is getting harder to spot, however, as machine-learning algorithms become better at emulating human behavior.

Apart from spreading fake news, misinformation campaigns can also divert attention from other, more serious problems. To combat such manipulation, we have recently developed a software tool called <u>Bot-Slayer</u>. It extracts hashtags, links, accounts and other features that co-occur in tweets about topics a user wishes to study. For each entity, BotSlayer tracks the tweets, the accounts posting them and their bot scores to flag entities that are trending and probably being amplified by bots or coordinated accounts. The goal is to enable reporters, civil-society organizations and political candidates to spot and track inauthentic influence campaigns in real time.

These programmatic tools are important aids, but institutional changes are also necessary to curb the proliferation of fake news. Education can help, although it is unlikely to encompass all the topics on which people are misled. Some governments and social media platforms are also trying to clamp down on online manipulation and fake news. But who decides what is fake or manipulative and what is not? Information can come with warning labels such as the ones Facebook and Twitter have started providing, but can the people who apply those labels be trusted? The risk that such measures could deliberately or inadvertently suppress free speech, which is vital for robust democracies, is real. The dominance of social media platforms with global reach and close ties with governments further complicates the possibilities.

One of the best ideas may be to make it more difficult to create and share low-quality information. This could involve adding friction by forcing people to pay to share or receive information. Payment could be in the form of time, mental work such as puzzles, or microscopic fees for subscriptions or usage. Automated posting should be treated like advertising. Some platforms are already using friction in the form of CAPTCHAs and phone confirmation to access accounts. Twitter has placed limits on automated posting. These efforts could be expanded to gradually shift online sharing incentives toward information that is valuable to consumers.

Free communication is not free. By decreasing the cost of information, we have decreased its value and invited its adulteration. To restore the health of our information ecosystem, we must understand the vulnerabilities of our overwhelmed minds and how the economics of information can be leveraged to protect us from being misled.

FROM OUR ARCHIVES

Confronting Misinformation. Special report; November 2020.

NEUROPLASTICITY

EXAMPLE 1

What hand transplants are teaching us about the brain

By Scott H. Frey

62 Scientific American, December 2020



HAND OF ANOTHER enables transplant recipient Donald Rickelman to hold and touch.

Scott H. Frey is Miller Family Professor of Cognitive Neuroscience at the University of Missouri-Columbia. He is author of an upcoming book on amputation, hand transplantation and the human brain.



N FEBRUARY 1964 ROBERTO GILBERT ELIZALDE, A MAYO CLINIC-TRAINED SURGEON in Guayaquil, Ecuador, found the ideal candidate for a radical procedure being developed in his laboratory. Julio Luna was a 28-year-old sailor who had lost his right hand in a grenade explosion. Gilbert Elizalde, inspired by the successful transplantation of a kidney harvested from a cadaver in the U.S., intended to replace Luna's missing appendage with a donor's.

For nine long hours Gilbert Elizalde and his team worked to prepare Luna's injured limb before skillfully marrying his bones, tendons, blood vessels, muscles, and skin with the forearm of a laborer who had died from a bleeding stomach ulcer. Using recently developed microsurgical techniques, the team stitched together the delicate, tubelike fascicles, nerve-surrounding sheaths that they hoped would guide sprouting sensory and motor nerves from Luna's injured forearm to reinnervate the new hand over the ensuing months.

Exhausted, the team watched nervously as the surgical clamps were released, and Luna's blood perfused his pale new hand to life. Long-distance congratulatory calls circulated. The news made the *New York Times:* "Dead Man's Hand Is Transplanted." The hand became one of the first human body parts to be transplanted, after the kidney and cornea. It was a long shot. "Several specialists who were questioned yesterday agreed that the odds against ultimate success were huge," the *Times* reported.

For the first week it looked like the skeptics might be proved wrong. When Luna contracted his forearm muscles, tendons in the new hand curled the fingers. Doctors gave Luna an early immunosuppressant, azathioprine, to stop his body from rejecting the foreign appendage. But in the second week it became clear that the immunosuppressant was not enough. When evidence of gangrene appeared, Luna was flown to Boston, where last-ditch efforts to save the hand failed. Twenty-three days after the transplant he became an amputee again.

The medical community both praised and condemned Gilbert Elizalde for this risky surgery. Critics called the procedure unethical, dangerous and unnecessary because it was not needed to save Luna's life—a position on hand transplantation that some experts still hold today. It took another three decades before hand transplantation received a second look.

Over those years surgical techniques evolved, and the development of more effective immunosuppressants (cyclosporine, followed by rapamycin and tacrolimus) allowed transplantation of certain solid organs—kidneys, livers, hearts—to become nearly routine. By the 1990s the success of these powerful pharmacological agents raised hopes of preventing rejection of transplants consisting of multiple tissue types muscle, skin, bone, nerve and vascular tissue. The field of composite tissue allotransplantation was born. In 1998 a team in France performed the second hand transplant in history, followed shortly thereafter by a group at Louisville's Jewish Hospital in Kentucky. That recipient, Matthew Scott, will soon celebrate the 22nd anniversary of his successful transplant.

Yet hand transplantation remains experimental and, in some circles, controversial. The procedure has been performed <u>only 100 or so times</u> worldwide. Unlike other organ transplants, hand transplantation does not save lives. Recipients undergo a major operation followed by a lengthy recovery and intensive rehabilitation. They face a lifetime regimen of immunosuppressant drugs that can be hard on internal organs and that can increase the risks of certain cancers, infections and other illnesses. Twelve years after receiving his transplant David Savage, whom I will tell you more about soon, lost his life to a cancer that may have been related to immunosuppression.

So why not just use a prosthesis? When I asked transplant recipient Erik Hondusky this question, his answer was simple: "It is a two-handed world." Hondusky's observation captures feelings expressed by other hand transplant recipients who also shared their

dissatisfaction with prosthetics and the strong desire to feel whole again. Prostheses remain insensitive tools; you cannot use them to feel the glance of a spiderweb, or the little bumps marking "F" and "J" on a keyboard, or tiny temperature changes in a cup of coffee. Sadly, Erik developed a staph infection that led to the amputation of his hand nine years after his transplant. He uses a prosthesis

reluctantly, only while riding his motorcycle.

Prosthetics come with their own challenges. Despite major advances in technology, a high percentage of amputees choose to give up their upper-extremity prostheses. Our longtime collaborator in Louisville, Christina Kaufman, notes that overall the record of surgical outcomes for hand transplants-and prevention of their rejection-remains impressive, with approximately 80 percent of recipients retaining the hand for at least five years. As techniques for matching immunologically compatible donors and recipients improve, this percentage is expected to grow, along with the number of recipients. Consequently, a successful transplant is no longer simply one that survives rejection. Instead success is increasingly defined based on the extent to which recipients develop functional use of their new hands. And that is where brain science comes into play.

AMPUTATION AND THE BRAIN

MY CURIOSITY about how the brain controls the hands began early, inspired by watching my mother struggle with everyday tasks as a result of her multiple sclerosis, a disease in which one's own immune system ravages the fatty myelin that surrounds neurons in the brain and spinal cord. Her loss of hand function, balance, muscle weakness and spasticity linger as vivid memories and have driven my quest to understand how the brain controls the hands. Our brains dedicate a vast amount of real estate to planning and controlling hand actions. For more than 20 years my lab has been exploring this territory. We investigate the neural mechanisms of hand movements with functional magnetic resonance imaging (fMRI), a technique that allows us to noninvasively assess brain function by tracking local fluctuations in blood flow and oxygenation levels that are coupled to local changes in neural activity.

On a practical level, here is how fMRI works: Imagine that you volunteer for a common (and painfully boring) fMRI experiment that involves alternating the tapping of your fingers interspersed with periods of rest. When moving the fingers on your right side, a population of specialized neurons in the hand region of your left motor cortex (each brain hemisphere controls movements and processes sensations of the opposite side of the body) produces descend-

Surgical outcomes for hand transplants are impressive—80 percent of recipients retain their new hands for at least five years.

ing impulses, called action potentials. These signals pass through the brain's subcortical structures and down the spinal cord before triggering peripheral motor nerves that cause the appropriate muscles of your right forearm and hand to contract. Specialized receptors in your skin, tendons and joints are stimulated by your finger movements and send feedback signals through peripheral sensory nerves to the spinal cord. There, ascending impulses are relayed via subcortical structures to a specific pool of neurons in the hand area of your left somatosensory cortex, which processes incoming sensory signals.

All of this activity consumes energy. Within fractions of a second tiny capillaries dilate and saturate more active areas of your brain with an excess of oxygen-rich blood (hemoglobin). Changes in local blood oxygen concentrations that accompany neural activity affect the fMRI's magnetic field. Without oxygen bound to it, hemoglobin is strongly attracted to a magnetic field in what is called a paramagnetic state, and oxygenated hemoglobin is weakly repelled (a diamagnetic state). These effects can be captured as a blood-oxygen-level-dependent signal tethered to neural activity. During the little finger-tapping experiment, the hand areas of your left motor and sensory cortices glow with activity on the scanner console.

FMRI can even detect this brain activity in some people whose hands have been amputated. Many amputees experience powerful illusory sensations of a "phantom limb," the sensation that the amputated appendage is still present. If a researcher asks a person with an amputation to move their phantom fingers, fMRI detects increased activity in the former hand areas. These findings suggest that the brains of at least some amputees retain a representation of the amputated hand even after the physical one is gone although the story is not quite that simple.

Decades of basic neuroscience research in animals show that the organization of the cerebral cortex changes profoundly when it is deprived of routine activity from a limb-the result of damage to the peripheral nerves. That is, maps of sensory and motor functions in the cortex depend on stimulation. At least in part, the same appears to be true for humans as well. When amputees perform a task with their remaining hand, they exhibit increased activity in sensory and motor cortical areas formerly devoted to the now missing hand. This involvement of the former hand areas occurs in addition to typical activity within those areas dedicated to the healthy hand. Similarly, some brain-imaging studies have shown that movements of the lips may also increase activity in the former hand areas of amputees.

This is where hand transplantation gets very interesting to a brain scientist. Does the mature human brain retain enough plasticity years or even decades after amputation in areas formerly devoted to the amputated hand to take on control of the transplanted hand? The answer to this question could have broad implications for understanding the potential for recovery of function following injuries to the body, spinal cord or even the brain itself.

BRAIN RECOVERY

I STARTED EXPLORING this issue when David Savage and his wife, Karen, traveled to my lab, then located at the University of Oregon, a mere four months after his hand transplant surgery at Jewish Hospital in Louisville. If ever there was a case to test the boundaries of post-transplant recovery, David's was it. As a young man, he lost his right hand in a shop accident, and before the transplant he had lived as an amputee for almost 35 years. While we talked, David unzipped the Velcro straps that held his removable splint in place and nonchalantly began opening and closing his new hand. When he saw the stunned look on my face, he cracked a smile, grasped my pen and wrote his name in my notebook. Immediately it became clear who was the professor and who was the student.

Before getting into David's exciting results, we need a short aside to discuss the workings of the peripheral nerves in your hand and arm. Unlike the brain or spinal cord, peripheral nerves are capable of regrowing when injured. They regrow quickly, too—at the astonishingly speedy rate of up to two millimeters per day. A skilled microsurgeon will prepare a patient for this regeneration by carefully segregating the fascicles that encompass the various nerve branches and then delicately suture them to matched fascicles in the donor hand. These fascicles surround vast numbers of microscopic axons—the slender projections growing from the cell bodies of individual neuronsmuch like conduits surrounding the bundles of multicolored phone wires you might see at a construction site. Once surgically joined, the fascicles guide sprouting motor axons toward hand muscles, where they form neuromuscular junctions. Similarly, axons that send sensory signals to the brain are steered toward the skin, tendons and joints. There sensory nerves produce specialized receptors sensitive to changes in pressure, vibration, and temperature. The process through which peripheral nerves grow back and rejoin the sensory network is called reinnervation.

But even a gifted microsurgeon has limited control over where individual peripheral nerve axons actually terminate in the donor hand. The upshot is that subsequent reinnervation errors present a challenge for recovery of hand function. In David's forearm, the regenerating sensory nerves had inched their way through the repaired fascicles. Along the way, some axons had veered off and innervated patches of skin on his new palm, forming numerous branches capped by tiny sensory receptors. We know this because at this early point in his recovery, David was able to detect and localize light touch along the base of his thumb even though the rest of his hand still lacked sensation. I could not help thinking about how remarkable that was. His brain was receiving input originating in peripheral nerves that had last carried sensory signals from a hand more than three decades ago. These impulses were arising from specialized receptors that had only recently set up camp in an entirely different hand.

Reinnervation error was an issue for David, but his brain still found ways to compensate. A sensory nerve in the forearm that once received input from a patch of skin located, say, on the base of his birth thumb might now carry signals arising from an entirely different location on his transplanted palm. Somehow, in a very short period, David's brain had, nonetheless, learned to interpret the new input it received correctly; if I probed his palm, he experienced the feeling as arising from there and not from his thumb. These perceptions were a few millimeters off but still remarkable considering that until recently David had no right hand for more than three decades. Exactly how the brain solves this puzzle remains unclear. Our working hypothesis is that through the repeated pairing of visual and tactile feedback-seeing and touching at the same time during hand use-brain mechanisms learn to correct for reinnervation error.

As if having waited patiently all this time for the opportunity to again process signals arriving from the hand, the appropriate area of David's sensory cortex responded vigorously when I gently brushed his transplanted palm during an fMRI scan. That is not to say, however, that postamputation reorganization had been fully reversed. As with other amputees, brushing the palm of David's intact left hand also elicited responses in this same area, the right sensory cor-

A Delicate Rewiring Act

Injuries to peripheral nerves can reshape the brain-to-hand command system that allows us to pick up a fork without a second thought. Hand transplant surgery to restore neural connections must contend with possible rewiring that may occur after an amputation.

To understand what can go awry, first consider what happens when a two-handed person moves one of the fingers on the right hand (A). Then compare typical functioning with three examples of what can occur when the hand is not there (B). Research suggests that the brains of at least some amputees retain a representation of the amputated hand even after the physical one is gone. But for many, the organization of the cerebral cortex is profoundly altered when deprived of activity by damage to the peripheral nerves.

B NEURAL PATHWAYS IN AMPUTEES

SCENARIO 1

In some cases, the

cortex also exhibits

increased activity

somatosensory

hand region of the left

Many amputees experience "phantom limb" sensations. If they are asked to "move" the finger that is no longer there or the former motor hand area is stimulated with a technique called transcranial magnetic stimulation, they report *feeling* phantom finger movements.

> Activated hand region of left motor cortex



To move a finger on the right hand, neurons in the hand region of the left motor cortex produce impulses that trigger motor nerves that cause muscles of the right forearm and hand to contract. Hand region of left motor cortex

Hand region of left somatosensory cortex

Returning sensory signals generated when the hand is moved travel to the hand area of the left somatosensory cortex, confirming the movement and conveying the new posture of the hand.

SCENARIO 2

Mouth regions of

the motor cortex

Mouth regions of the

somatosensory cortex

Signals can get literally crossed. In some amputees, the "hand" region of the cerebral cortex activates when the person moves their lips. Activity increases not only within the expected motor and sensory face areas but also in sites that controlled hand movement before the amputation, on the opposite side of the brain from the injury.

Hand region of left somatosensory

cortex and left motor cortex

SCENARIO 3

When performing tasks that involve their intact hands, amputees show increased activity within the appropriate neural hand areas, as well as those previously devoted to the amputated hand located on the opposite side of the brain.

Hand regions of motor cortex (*right* and *left*) —

Hand regions of somatosensory cortex (*right* and *left*) —



DEXTROUS MOVEMENT with Rickelman's transplanted hand allows the effortless buttoning of his shirt. tex. But he never showed any uncertainty about whether these sensations were coming from his intact or transplanted hand.

David eventually succumbed to cancer, but a transplanted hand can last for decades without any apparent consequences. At more than 21 years postsurgery Matthew Scott—the first case performed in Louisville has kept his transplanted hand longer than anyone else who has had this operation. He spent 13 years as an amputee after losing his dominant left hand in a fireworks accident that occurred in his 20s. Matt visited us in 2008, nine and a half years after his operation. Feeling had long ago emerged throughout his new hand, indicating that regenerating sensory nerves had completed their journey. He localized touch at all locations on his transplanted hand; on average, he was only a few millimeters less accurate than on his uninjured one. We created a computer-controlled system to stimulate the tips of his fingers during an fMRI session, which revealed distinct maps of each individual digit within the hand area of his sensory cortex.

Although I am tempted to conclude that the organization of Matt's sensory cortex had sprung back to its preamputation organization, this conjecture would be overreaching. We lack data on his brain prior to his amputation, and the fact is that we all have slight differences in the fine-grained organization of our brains, which result from genetics and differing life experiences. We can safely say that Matt's sensory cortex appears to contain a map of his transplanted hand that is within the range of natural variation that we observe in healthy adults. Still, even eight years' post-transplant Matt's brain showed

lingering evidence of his amputation. Stimulating his intact right hand also increased activity within the former hand area. How then can his hand function be so good? Part of the answer may involve contributions from other brain regions, located upstream from the hand regions, that are not directly involved in sensing and motor functions.

Simple tasks such as finger tap-

ping or passively experiencing touch are useful means to probe the organization of the motor and sensory cortices. Everyday life, however, requires the ability to grasp and manipulate objects. These more complex, goal-directed actions involve areas of the brain involved with higher-level processing, such as the parietal and premotor areas. These cortical regions use multisensory information about the properties of the object and the positioning of one's body to plan movements targeted to a specific goal, such as grasping a cup to take a drink.

Ken Valyear led a project in our lab that used motion capture and fMRI techniques to study the recovery of visually guided grasping in transplant recipient Donald Rickelman, who had lived as a lefthand amputee for 14 years after losing his hand in an industrial accident. We were particularly interested in the role of the anterior intraparietal cortex (aIPC) a small region located just behind the sensory hand area that is involved in properly shaping the hand to conform to the perception of objects' shapes, orientations and sizes.

At both 26 and 41 months after receiving his transplant, Donnie, like the other transplant recipients we have studied, showed evidence of persistent reorganization in his motor and sensory hand areas. Not surprisingly, he also experienced impediments in some basic hand functions. Detailed analyses of his hand motions, captured at high resolution as he reached for and grasped objects, revealed substantial improvements in coordination over this same period. How was he compensating for his motor and sensory impairments? To find out, we built a special apparatus that allowed us to ask this question with fMRI. When Donnie grasped objects at 26 months posttransplant, his aIPC and premotor cortex showed weak levels of grasp-related activity relative to people with intact limbs. At 41 months patterns of grasprelated activity had increased within the aIPC and premotor cortex and more closely resembled those of control subjects. We speculate that his improved ability to reach and grasp with his transplanted hand over time may be linked to these higher-level regions picking up the slack for the lagging performance of his reorganized motor and sensory areas.

Donnie and Matt continue to improve their sensory and motor functions many years after receiving

Work with hand transplant recipients challenges fundamental notions about the limits of neuroplasticity in mature adults.

their transplants, suggesting that the learning-related changes in the brain may continue to contribute to recovery long after the peripheral nerves have fully regenerated. A major goal of our current work is establishing the relationship between such experience-dependent changes in the brain and use of the hands during real-life activities as measured using wireless wearable sensor technology. These devices allow us to observe at high resolution hand and prosthesis activity over numerous days as participants go about their ordinary lives.

If the superpower of the peripheral nerves is their ability to regenerate when injured, the brain's is its capacity to reconfigure itself in response to changes in stimulation. Both play complementary roles in recovery from bodily injuries. Though in its infancy, work with hand transplant recipients is already showing us that the human brain can respond to the reinstatement of stimulation even after many years of deprivation. These findings challenge fundamental notions about the limits of neuroplasticity in mature adults and may give hope to those struggling to overcome the effects of amputation and other devastating bodily injuries. It may indeed be possible to reinstate the grasping and touch that had been lost decades earlier.

FROM OUR ARCHIVES

Tomorrow's Prosthetic Hand. Jessica Schmerler and Ian Chant; Scientific American Mind, July 1, 2016.

scientificamerican.com/magazine/sa

DOUGHNUT DEVICE: Engineers work on the first section of the vacuum vessel-the torusshaped container that will house the plasma where, ideally, fusion will ignite. Inside ITER, two isotopes of hydrogendeuterium and tritiumwill collide at high speed, offering a chance for two atoms to stick and form helium. The small bit of mass lost in the reaction converts into energy in a deal brokered by Albert Einstein's famous equation, $E = mc^2$.

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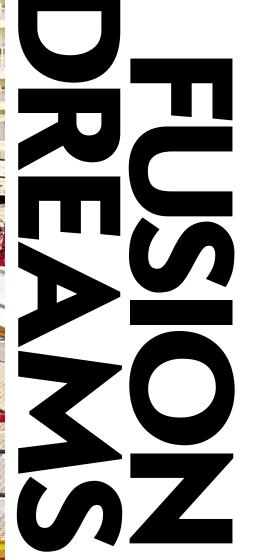


PHYSICS

Assembly has begun on ITER, the world's largest nuclear fusion reactor

By Clara Moskowitz

Photographs by Manuela Schirra and Fabrizio Giraldi



Clara Moskowitz is a senior editor at *Scientific American*, where she covers space and physics.



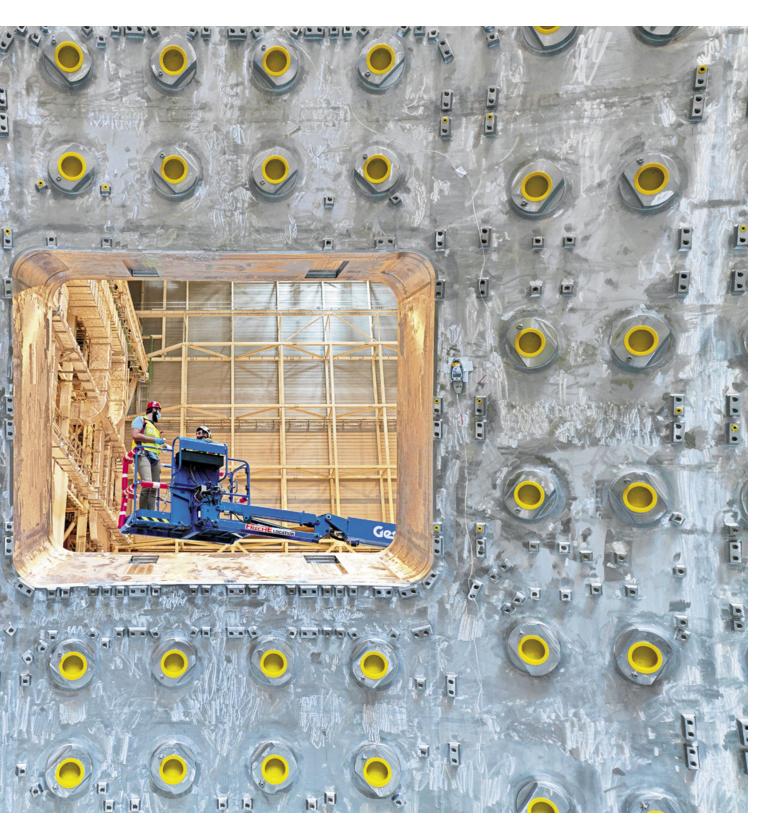
HUMANS ARE AN ENERGY-HUNGRY SPECIES, AND OUR current sources of power are not cutting it. Nuclear fusion, the process that fuels the sun, might offer the kind of clean, abundant energy we need if only scientists can figure it out. The International Thermonuclear Experimental Reactor (ITER) is the biggest and most ambitious attempt yet to harness the energy produced by forcing two atoms to become one. The \$25-billion experiment in Saint-Paul-lez-Durance, France, is a joint project of the European Union, China, India, Japan, South Korea, Russia and the U.S. Its ultimate goal is to do what no fusion experiment has done before: produce more heat than it consumes.

The project has been stymied by delays and ballooning costs, and a critical independent assessment forced out the top leadership several years ago. In some skeptics' eyes, it will always be a boondoggle, a waste of too much time and money for an experiment that is aiming to be not even a working power plant but merely a proof of concept. But ITER finally reached a long-sought milestone in July 2020 with the official start of machine assembly—when scientists began joining the various components provided by the partner countries. "We have the same feeling as somebody who is supposed to run successive marathons, and you achieve the first one, but still you know there are many more to do," says Bernard Bigot, who took over as ITER director general in 2015. "It gives us more confidence in the future, but we know that nothing is [taken] for granted."

The challenge is to essentially build a miniature star inside a laboratory—and then control it. The heart of the experiment is a 23,000-ton cylinder where intense superconducting magnets will try to keep a 150-million-degree-Celsius plasma contained long enough for fusion to occur. Making the physics work out will be a huge challenge, but so will conquering the construction. "It is a largescale international project where parts are made all across the world, and it has to fit together like a puzzle, and it has to work," says plasma physicist Saskia Mordijck of William & Mary, who is not part of the ITER team.

Scientists hope to press the proverbial red button and turn on the reactor in 2025, with the ultimate goal of running it at full power by 2035. If it succeeds, the payoff would be gigantic. Fusion has the potential to release much more energy than burning coal or oil or even nuclear fission, which fuels traditional nuclear power plants. Fusion produces no greenhouse gases or radioactive waste. "Fusion from my point of view is really the one option that complements reusable energy and could be the solution for climate change," Bigot says. "The next three or four years will be absolutely critical."





TEMPERATURE GRADIENT: ITER will include one of the hottest places in the universe—the vacuum vessel housing the 150-million-degree-Celsius plasma—as well as one of the coldest places in the universe; the magnets that will confine and control that plasma must be kept at about four kelvins (-269 degrees C). Separating the two will be a beryllium-coated steel "blanket" to shield the sections from each other, which will attach to the vacuum vessel's interior wall via stub keys, currently covered by yellow caps to keep off dust.



WORLD'S LARGEST: The tokamak chamber, seen from the top (1) and middle (2), is a cylinder that will hold the ITER experiment. The word "tokamak" is a Russian acronym for a "toroidal chamber with magnetic coils"—a concept first developed in 1957 by physicist Igor Golovin. ITER's tokamak will be the biggest ever built, twice the size of the largest currently operating. The base of the machine was lowered into the chamber in July 2020, marking the beginning of the project's assembly at the site in the south of France. The site is funded by Europe, which is paying for nearly half of the total cost of the project; Europe's contribution is managed by Fusion for Energy.



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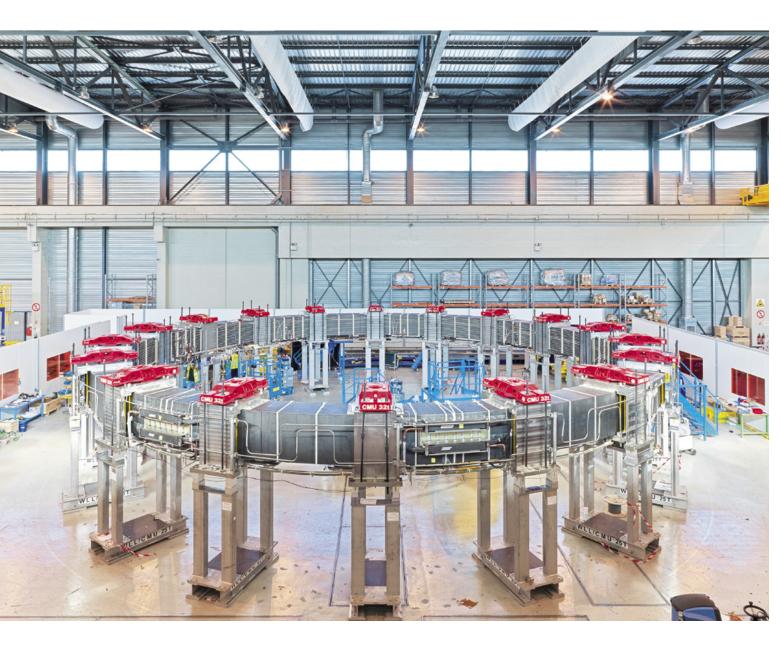
EMPTY VESSEL: ITER's vacuum vessel will be made of six segments, each built in South Korea or Italy. The huge steel sections had to be shipped by boat to the port of Fos-sur-Mer near Marseille, where they were transported by road 100 kilometers northeast to the ITER site. Now that the first pieces have arrived, workers will connect them with magnets and thermal shields and then lower them into the tokamak chamber (1).

DEEP FREEZE: The superconducting magnets in the reactor can work only at supercold temperatures near absolute zero, which will be maintained by liquid helium circulating through cryogenic pumps. Operators control the system via a complex set of hand valves (2) based on local readings of pressure, temperature and flow. The finished cryogenic plant, built by contractor Air Liquide (3), will be the world's largest helium-refrigeration unit.



NOTADOUBRE

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MAGNETIC CAGE: ITER's fusion plasma will be encased and contained by a nest of magnets, including six ring-shaped superconducting poloidal magnets (*shown here*) that will pile on top of one another horizontally to surround the plasma. In addition, 18 toroidal field coils will encircle the machine vertically, and one large central solenoid will sit in the middle, forming the largest superconducting magnet system ever built. Superconductors allow electric current to flow without resistance, enabling electrons to move freely to create intense magnetic fields. MAGNET CONSTRUCTION: Made of niobium-tin and niobiumtitanium, the poloidal magnets are the only ITER components manufactured on-site. With diameters between 17 and 24 meters and weighing up to 400 metric tons each, they are too large to be built elsewhere and transported. Poloidal Field Coil #6 is shown here inside its cooling cryostat.



FROM OUR ARCHIVES

Fusion's Missing Pieces. Geoff Brumfiel; June 2012.

scientificamerican.com/magazine/sa

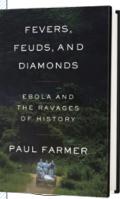
By Andrea Gawrylewski

Fevers, Feuds, and Diamonds:

Ebola and the Ravages of History

by Paul Farmer. Farrar, Straus and Giroux, 2020 (\$35)

At the end of June the World Health Organization declared that the 10th outbreak of Ebola in the Democratic Republic of Congo was officially over, after two years and



2,287 deaths. It was the latest severe outbreak and most likely not the last. In this riveting first-person account of the even deadlier 2013-2016 outbreak in West Africa, Farmer, the renowned American physician and founder of Partners in Health, lays out both an intimate look and a 10,000-foot view of the dire public health situation there. A history of colonial oppression, exploitation by mining interests and racism has contributed to civil war and poverty. Such unrest, he argues, has led to socalled medical deserts, whereby disease treatment is limited and survival rates are tragically low, compared with richer nations. Arriving in West Africa in the midst of the outbreak in 2014, Farmer recounts the difficult clinical circumstances faced by local Ebola treatment units and

weaves in the stories of local doctors and survivors who played a central role in confronting the terrible disease.

The Janus Point:

A New Theory of Time by Julian Barbour. Basic Books, 2020 (\$32)



Imagine a cosmos in which the arrow

of time flies backward. Mountains rise from windblown dust. Decrepit bodies bob

up from graves, becoming youthful before shrinking to disappear inside a mother's womb. Planets, stars and galaxies dissolve into glowing, dense plasma that pervades a collapsing universe. In all things, disorder gives way to order-entropy inexorably decreases-rather than vice versa, as in the everyday reality we experience. As farfetched as all this seems, in The Janus Point, physicist Barbour argues with poetic erudition for a solution to the vexing problem of time's apparent one-way flow: a mirrorlike temporal duality in which the big bang is not an explosive cosmic beginning but rather ' a special point on the time line of the universe." -Lee Billings

The Organ Thieves: The Shocking Story of the First Heart Transplant in the Segregated South

by Chip Jones. Gallery Books/Jeter Publishing, 2020 (\$28)



Black Americans receive inferior health care on all scores—from general wellness checks to treatment for chronic illness, which leads to worse health outcomes.

They are 60 percent more likely to be diagnosed than white people with diabetes, for example, and 40 percent more likely to be diagnosed with hypertension. The roots of this inequity are firmly rooted in racism, not race, writer Jones shows in this gripping book. Examples go back to the earliest days of the U.S.—he recounts the legal battles that arose in the 18th century and later over body snatching from Black graveyards for medical research. In 1968 doctors extracted, without his consent, the beating heart of Black factory worker Bruce Tucker for transplant into a white businessman, after Tucker suffered a head injury. Sadly, such disregard for patients' rights is not reserved for history.

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Copies not distributed (see instructions to publishers #4 (page #3)): average number of copies of each issue during preceding 12 months: 83,173; number of copies of single issue published nearest to filing date: 53,065. h. Total (sum of 15f and 15g): average number of copies of each issue during preceding 12 months: 332,967; number of copies of single issue published nearest to filing date: 288,072. *i*. Percent paid (15c divided by 15f times 100): average number of copies of each issue during preceding 12 months: 98.2%; number of copies of single issue published nearest to filing date: 99.9%. 16. Total circulation does not include electronic copies. 17. Publication of statement of ownership: If the publication is a general publica-tion, publication of this statement is required. Will be printed in the December 2020 issue of this publication. 18. I certify that all information furnished on this form is true and complete. 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Naomi Oreskes is a professor of the history of science at Harvard University. She is author of *Why Trust Science?* (Princeton University Press, 2019) and co-author of *Discerning Experts* (University of Chicago, 2019).

History Matters to Science

It helps to explain how cynical actors undermine the truth

By Naomi Oreskes

2020 has been a historic year—and mostly not in a good way. Among many things, we saw a historic level of disregard of scientific advice with respect to the COVID-19 virus, a disregard that made the pandemic worse in the U.S. than in many other countries. But while the events of 2020 may feel unprecedented, the social pattern of rejecting scientific evidence did not suddenly appear this year. There was never any good scientific reason for rejecting the expert advice on COVID, just as there has never been any good scientific reason for doubting that humans evolved, that vaccines save lives, and that greenhouse gases are driving disruptive climate change. To understand the social pattern of rejecting scientific findings and expert advice, we need to look beyond science to history, which tells us that many of the various forms of the rejection of expert evidence and the promotion of disinformation have roots in the history of tobacco.

Throughout the first half of the 20th century, most Americans saw science as something that made our lives better. Science had deepened our understanding of the natural world, which helped us to cure diseases, light our homes and bring new forms of entertainment into our lives. Perhaps most important, physicists helped to win World War II and became cultural heroes. Chemists got their due, too. As DuPont reminded us, we had "<u>better</u> things for better living through chemistry." At General Electric, scientists and engineers were helping to "<u>bring good things to</u> <u>life</u>." These were not just slogans; corporate R&D really did produce products that measurably improved many American lives. But corporate America was also developing the playbook for science denial and disinformation.

The chief culprit in this darker story was the tobacco industry, whose playbook has been well documented by historians of <u>science</u>, technology and medicine, as well as <u>epidemiologists</u> and <u>lawyers</u>. It disparaged science by promoting the idea that the link between tobacco use and lung cancer and other diseases was uncertain or incomplete and that the attempt to regulate it was a threat to American freedom. The industry made products more addictive by increasing their nicotine content while <u>publicly denying</u> that nicotine was addictive. With these tactics, the industry was able to delay effective measures to discourage smoking long after the scientific evidence of its harms was clear. In our 2010 book, *Merchants of Doubt*, Erik M. Conway and I showed how the same arguments were used to delay action on acid rain, the ozone hole and climate change—and this year we saw the spurious "freedom" argument being used to disparage mask wearing.

We also saw the tobacco strategy seeping into social media,



which influences public opinion and which many people feel needs to be subject to greater scrutiny and perhaps <u>government</u> regulation. In October 2019 Congress held hearings to investigate the role of Facebook in potentially spreading misinformation. In the summer of 2020 a <u>report</u> from civil-rights law firm <u>Relman</u> <u>Colfax</u> suggested that Facebook posts could contribute to voter suppression. Climate scientists have <u>complained</u> that the social media giant contributes to the spread of climate denial by permitting false or misleading claims while hobbling responses by mainstream scientists by labeling their posts "political."

Without a historical perspective, we might interpret this as a novel problem created by a novel technology. But this past September, a former Facebook manager <u>testified</u> in Congress that the company "took a page from Big Tobacco's playbook, working to make our offering addictive," saying that Facebook was determined to make people addicted to its products while publicly using the euphemism of increasing "engagement." Like the tobacco industry, social media companies sold us a toxic product while insisting that it was simply giving consumers what they wanted.

Scientific colleagues often ask me why I traded a career in science for a career in history. History, for some of them, is just "dwelling on the past." But, as the bard said in *The Tempest*: "What's past is prologue." If we are to confront disinformation, the rejection of scientific findings, and the negative uses of technology, we have to understand the past that has brought us to this point.

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Steve Mirsky was the winner of a Twist contest in 1962, for which he received three crayons and three pieces of construction paper. It remains his most prestigious award.



The Real Deal

As Bugs Bunny once said, "Last look!"

By Steve Mirsky

Back in 2010, we celebrated the life of Martin Gardner, who died that year at the age of 95. He wrote the Mathematical Games column for *Scientific American* magazine for nearly 25 years, and he remains the gold standard for this publication's columnists.

Upon Gardner's death, I interviewed his friend and protégé Douglas Hofstadter, the Pulitzer Prize-winning author of *Gödel, Escher, Bach: An Eternal Golden Braid.* The book came out in 1979, when Hofstadter was 34. Which meant that in 2010 he was 65. And it struck me that it should take much longer to go from 34 to 65 than a mere 31 years. It really should take more like 50 years to go from being 34 to 65, I thought, even though the arithmetic regarding that transition was inarguably ironclad.

In a somewhat related vein, this issue of *Scientific American* marks 25 years since the first appearance of Anti Gravity. In 1995 I was 37 years old and in my salad days, when I was green in judgment. And in only 25 years I've turned into an *alte kaker*. I'm still green, but now it's because of digestive issues.

Horror movie maven David Cronenberg captured the weirdness of this fast-forwarding in the introduction to a 2014 English translation of Franz Kafka's The Metamorphosis: "I woke up one morning recently to discover that I was a seventy-year-old man. Is this different from what happens to Gregor Samsa in The Metamorphosis? He wakes up to find that he's become a near-human-sized beetle Our reactions, mine and Gregor's, are very similar. We are confused and bemused, and think that it's a momentary delusion.... These two scenarios, mine and Gregor's, seem so different, one might ask why I even bother to compare them. The source of the transformations is the same, I argue: we have both awakened to a forced awareness of what we really are, and that awareness is profound and irreversible; in each case, the delusion soon proves to be a new, mandatory reality, and life does not continue as it did."

The previous more than 300 words of throat clearing is to set up the announcement that I'm hanging up my spikes. Well, in truth I hung up the spikes a very long time ago, when other kids my age started throwing breaking pitches. So let's say I'm hanging up my keyboard.

I'll still be making bad puns and snide remarks, of course, and I'll be ranting about antiscience politicians, but it'll mostly be just for the benefit, if you can call it that, of my wife and cats. Although it's not impossible that I may return to these pages from time to time when said wife and cats inform

me that I really should share my golden nuggets of insight with a wider audience if that will get me out of the living room.

By the way, I'd be remiss if I didn't note that the greatest commentary on *The Metamorphosis* occurs in Mel Brooks's 1967 movie *The Producers*, when the title characters are looking for the worst play in the world in order to guarantee a flop so they can keep most of the million dollars they raise rather than spend it on the production. Max Bialystock, brilliantly played by Zero Mostel, opens one of the hundreds of manuscripts around him and says, "'Gregor Samsa awoke one morning to discover that he had been transformed into a giant cockroach.' It's too good." Which in fact it was.

Back to Cronenberg and his "mandatory reality." In 2002 a White House official scoffed at journalist Ron Suskind for being in "the reality-based community." The official explained, according to Suskind, "We're an empire now, and when we act, we create our own reality."

I had two responses to that anecdote and attitude then that I hold to today, as the current White House's relationship with reality seems literally psychotic. First, *Scientific American* is the voice of the reality-based community. Second, if you think you create your own reality, real reality will come back to bite you in the ass.

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50, 100 & 150 YEARS AGO INNOVATION AND DISCOVERY AS CHRONICLED IN SCIENTIFIC AMERICAN

Compiled by Dan Schlenoff

In Vitro Progress "In laboratories at the Oldham General Hospital in Lancashire and at the University of Cambridge, human eggs have now been successfully brought to maturity, fertilized in vitro and cultured in vitro to the blastocyst stage of development, which is the stage immediately preceding the beginning of normal implantation of the fertilized egg in the uterus. Clinically it should be possible with these procedures to circumvent certain causes of infertility and to avert the development of embryos that otherwise could be expected to grow abnormally. Still further possibilities can be imagined. Eggs fertilized in the laboratory and cultivated to the blastocyst stage could be transferred back to the mother with an excellent chance of completing development normally. -R. G. Edwards and Ruth E. Fowler" The first baby to be conceived by in vitro fertilization was born at Oldham hospital in July 1978.

Battleship vs. Torpedo Plane

"Commenting on articles in the New York Tribune in which the abandonment of the superdreadnaught battleship was advocated, Rear Admiral Fiske says that most of the men who oppose the strenuous development of aeronautics have not carefully studied its possibilities. He believes with many others that aeronautics is destined to

DECEMBER







EPIC TALES

bring about 'a revolution in warfare, in comparison with which the revolution brought about by the invention of the gun was like a vaudeville performance.' Pretty strong words these for an admiral!"

After Currency Collapses

"One development of the impasse in import and export business between Germany and other countries growing out of the depressed value of the German mark is a modification of the barter system. Arrangements have been made by various British cotton interests who have arranged to furnish German cotton mills with raw cotton and take from them cotton yarn manufactured therefrom, the German manufacturers retaining a portion of the yarn as their payment for the use of their plant, of their labor, and other costs of manufacture."

O "This whole business of spiritualism has been the source of much mischief, and has brought insanity into many a family. Our readers ought to know, that no man of science, no sane man of intelligence has any faith in it. Before the light of science the whole thing is shown to be an imposition. But, as Dr. William A. Hammond savs: 'Spiritualism is a religion. As such it is held tenaciously by many well-meaning people. To reason with these would be a waste of words, just as much as would be the attempt to persuade



1870: A design for a convenient all-weather mailbox.

a madman out of his delusion. Emotion, or interest, or accident might change them, but facts never."

Patents for Post

"In attaching letter-boxes to lamp posts, this box is constructed in two hemispherical sections. The drop holes are made without movable lids, being protected by a projecting shield, as shown. This is a great convenience, as the use of one hand only is required to insert letters. The closing of an umbrella in a rain storm, or the setting down of a basket or a child in arms, in order to put a letter in the box, is thus obviated. Patented, through the Scientific American Patent Agency by Albert Potts, of Philadelphia, Pa."



U.S. Postal Service

In 1775 Benjamin Franklin was appointed the U.S.'s first postmaster general. Letters and more important for Scientific American—periodicals have been keeping citizens informed and engaged in the democratic process ever since. Two years after this magazine was founded in 1845, the U.S. Post Office started issuing postage stamps as a convenient way to pay for mailed items. This "folly" was decried by our forebears: delivery of the publication now had to be prepaid instead of being paid for by the recipient. The volume of mail has grown with the evolution of the technology to collect, sort and deliver it. In 1895 five billion

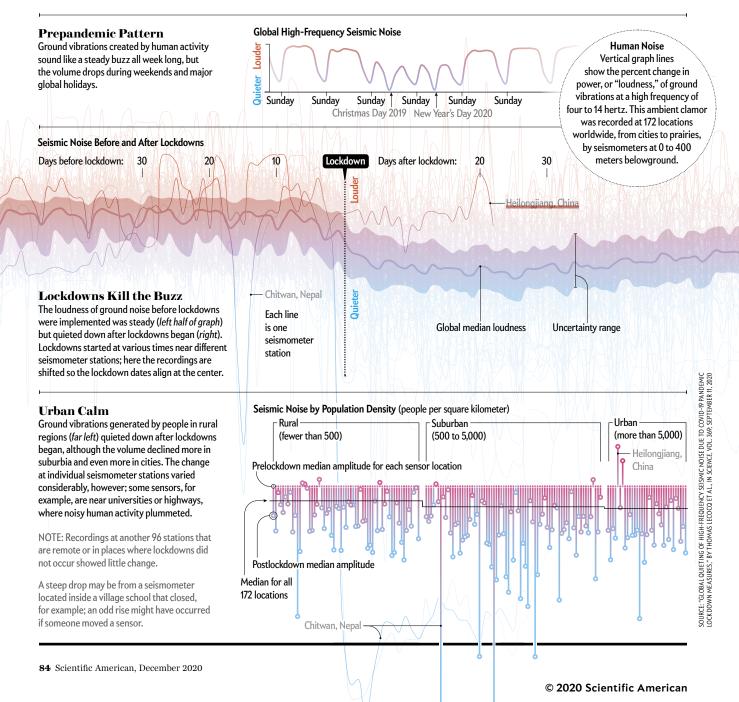
1896: Systems, people power and a few machines join forces to sort the mail.

pieces of mail went through sorting offices such as the one pictured at the left; by 2019, even in the era of e-mail, FedEx and UPS, 143 billion pieces of mail were delivered. -D.S.

COVID-19 Quiets the Earth

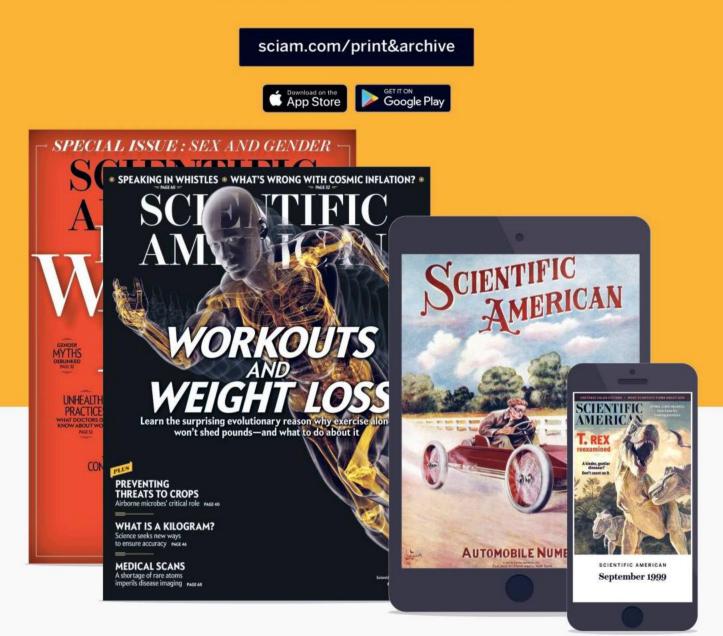
Seismic noise dropped worldwide as humans locked down

Earthquakes send strong tremors through the earth's crust, recorded by seismometers planetwide. Human bustle also creates an ongoing, high-frequency vibration—a background buzz—in the rock. After cities, states and countries implemented lockdowns to try to slow the spread of COVID-19 this past spring, the volume of human ground noise fell by up to 50 percent on average in various regions, as people stayed home instead of taking cars, buses and trains to work and school and as businesses and industries curtailed operations. The decline, evident for months, was recorded by seismometers as deep as 400 meters underground. "We were surprised," says seismologist Stephen Hicks of Imperial College London, "that noise from daily human activity penetrated that far down."



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